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BASELINE ECOLOGICAL RISK ASSESSMENT APPENDIX D: TOXICITY PROFILES AND TOXICITY REFERENCE VALUES

Newark Bay Study Area

Newark, New Jersey

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CONTENTS

TABLES

ACRONYMS AND ABBREVIATIONS

%	percent
µg/kg	microgram per kilogram
µg/L	microgram per liter
2,3,7,8-TCDD	2,3,7,8-tetrachlorodibenzo-*p*-dioxin
ACR	acute to chronic ratio
AhR	aryl hydrocarbon receptor
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
BERA	baseline ecological risk assessment
BTAG	Biological Technical Assistance Group
bw/day	body weight per day
COPEC	constituent of potential ecological concern
(CH3)2AsO(OH)	demethylarsinate
(CH3)3AsCH2COOH	arsenobetaine
CH3AsO(OH)2	monomethylarsonate
DASS	Diamond Alkali Superfund Site
DDD	dichlorodiphenyldichloroethane
DDE	dichlorodiphenyldichloroethylene
DDT	dichlorodiphenyltrichloroethane
dioxin	polychlorinated dibenzo-*p*-dioxin
dw	dry weight
Eco SSL	ecological soil screening level
ED10	effective dose at 10%
ERED	Environmental Residue-Effects Database
FIR	food ingestion rate
furan	polychlorinated dibenzofuran
HCB	hexachlorobenzene
HPAH	high molecular weight polycyclic aromatic hydrocarbon
HQ	hazard quotient
hr	hour
kg/day	kilogram per day

kg/L	kilogram per liter
LCL	lower confidence limit
LD50	lethal dose to 50%
LOAEL	lowest observed adverse effect level
LPAH	low molecular weight polycyclic aromatic hydrocarbon
LPR	Lower Passaic River
LPR FFS	Focused Feasibility Study Report for the Lower Eight Miles of the Lower Passaic River
LPRSA	Lower Passaic River Study Area
LPRSA BERA	Lower Passaic River Study Area Baseline Ecological Risk Assessment
MFO	mixed-function oxidases
mg/kg	milligram per kilogram
mg/L	milligram per liter
mg/m3	milligram per cubic meter
mmHg	millimeter of mercury
NAS	National Academy of Sciences
NBSA	Newark Bay Study Area
NOAEL	no observed adverse effect level
NRCC	National Research Council of Canada
OU	operable unit
PAH	polycyclic aromatic hydrocarbon
PCB	polychlorinated biphenyl
ppb	part per billion
ppm	part per million
SLERA	screening-level ecological risk assessment
SSD	species sensitivity distribution
SSL	soil screening level
TEF	toxic equivalency factor
TEQ	toxic equivalent
total DDx	sum of all six DDT isomers (2,4′-DDD, 4,4′-DDD, 2,4′-DDE, 4,4′-DDE, 2,4′-DDT and 4,4′-DDT)
TRV	toxicity reference value
UCL	upper confidence limit

USEPA	U.S. Environmental Protection Agency
Windward	Windward Environmental LLC
ww	wet weight

1 INTRODUCTION

This appendix presents toxicity profiles, selected toxicity reference values (TRVs), and the uncertainties associated with TRVs for the constituents of potential ecological concern (COPECs) identified in the Newark Bay Study Area (NBSA) Baseline Ecological Risk Assessment (BERA). The toxicity profiles are brief summaries regarding key ecotoxicological information on each chemical or chemical group identified as COPECs for the NBSA and help to inform the identification of TRVs for the receptors of concern evaluated in the BERA. These include the following:

- Benthic invertebrates (primarily epibenthic softshell clam [*Mya arenaria*] and blue crab [*Callinectes sapidus*])
- Fish (forage and predatory species at different trophic levels)
    - Mummichog/killifish (*Fundulus spp.*)
    - American eel (*Anguilla rostrata*)
    - Summer flounder (*Paralichthys dentatus*)/winter flounder (*Pseudopleuronectes americanus*)
    - White perch (*Morone americana*)
- Birds (benthivorous, omnivorous, and piscivorous water birds)
    - Spotted sandpiper (*Actitis macularius*)
    - Great blue heron (*Ardea herodias*)
    - Lesser scaup (*Aythya affinis*)
    - Double-crested cormorant (*Phalacrocorax auritus*)
- Mammals (semi-aquatic omnivores and predators)
    - Muskrat (*Ondatra zibethicus*)
    - River otter (*Lontra canadensis*)
    - Harbor seal (*Phoca vitulina*).

Toxicity profiles summarize characteristics of the COPEC that influence the fate, transport, and toxicity of the chemical/compounds and discuss what is generally known about potential toxicity to the various receptor groups. These profiles are generated through a review of the available scientific literature, but much of the information is acquired/excerpted from existing comprehensive toxicological profiles such as those prepared by the Agency for Toxic Substances and Disease Registry (ATSDR), and the *Handbook of Chemical Risk Assessment: Health Hazards to Humans, Plants, and Animals, Vol. 1-3 (Metals, Organics, Metaloids/Radiation, Index)* by Eisler (2000).

The TRVs are the specific effect thresholds identified and selected to assess tissue- and/or dietary-based risks using the standard risk calculation hazard quotient (HQ) approach, as described in BERA. The TRVs typically include two benchmarks: lowest observed adverse effect levels (LOAELs) and no observed adverse effect levels (NOAELs).

General TRV uncertainties, called out in the respective tables throughout this Appendix as "Key Uncertainties," are discussed in further detail in Section 19. Specific uncertainties with each TRV, if considered significant, are provided with the discussion of the basis of the TRV.

This report summarizes the basis of the TRVs, many of which came from the Lower Passaic River Study Area Baseline Ecological Risk Assessment (LPRSA BERA; Windward Environmental LLC [Windward] 2019) and the Focused Feasibility Study Report for the Lower Eight Miles of the Lower Passaic River (LPR FFS; U.S. Environmental Protection Agency [USEPA] 2014), as described in Section 3.5.2 of the BERA Report. The use of the same TRVs is based on the goal of maintaining, to the extent practicable, consistency with the technical approach and applications for estimating risks and drawing risk conclusions for the other operable units (OUs) of the Diamond Alkali Superfund Site (DASS), primarily the LPRSA BERA for OU4 (Windward 2019) and also the LPR FFS (USEPA 2014) for OU2. Unique TRVs for the NBSA were developed only for COPECs that were not assessed in the LPRSA BERA. In most cases, the alternate values were selected from the substantial list of studies that are included in the TRV database that was developed as part of the LPRSA BERA (Windward 2019, Appendix A, Appendix E). The derivation of the LPRSA TRVs that were adopted for this NBSA BERA are summarized in this appendix by COPEC and receptor. Additional details on their derivation is provided in Appendix A (specifically Section A-3) of the LPRSA BERA (Windward 2019).

For some receptors and COPECs, additional literature searches were performed to identify appropriate TRVs, as described in Sections 2 through 18 below. The toxicity studies that were evaluated for use in the BERA (LPRSA and NBSA) were considered acceptable for use in TRV derivation if they met the following requirements:

- The toxicity data were based on endpoints that directly measure survival, growth, or reproduction
- Toxicity effect levels were representative of NOAEL and/or LOAEL concentrations or doses
- The toxicity studies were conducted in a controlled environment using standardized and/or peer-reviewed experiment methods, in which a clear concentration- or dose-response relationship was reported
- The toxicity studies were based on the exposure of an organism to a single chemical or specific mixtures of related chemicals (i.e., mixtures of chemicals within the same class, such as PCBs)
- The toxicity data reflected a preferred exposure route relevant to the TRV type (e.g., ingestion exposure for dietary TRVs)
- TRVs were not based on bioaccumulation studies that did not measure effects on an appropriate endpoint (i.e., survival, growth, or reproduction).
- For regulated metals, acceptable LOAELs associated with adverse effects had to be above the optimal nutritional concentration for the species
- Unless no other data were available, TRVs for birds were not based on egg productivity or other reproductive endpoints in a domesticated species, such as chickens or Japanese quail, because of the differences in reproductive physiology (i.e. high egg-laying rates) between these species and wild bird species
- For tissue, TRVs were based on whole-body or egg tissue concentrations that were reported at the time that the effects were measured. Studies that did not report measured tissue concentrations were not considered, unless no other studies were available and a tissue concentration could be estimated

through the use of water or sediment exposure concentrations and bioconcentration factors reported in the study.

Table D-1a lists the NBSA COPECs, and Table D-1b compares the COPECs list between the NBSA (OU3), the LPRSA BERA (OU4; Windward 2019), and LPR FFS (OU2; USEPA 2014).

Table D-1a COPECs Evaluated for Shellfish, Fish, and Wildlife Receptors in the BERA

COPEC	COPECs for the NBSA BERA						
	Benthic Invertebrate Tissue	Fish Tissue	Fish Egg	Fish Diet	Bird Egg	Bird Diet	Mammal Diet
Dioxins/Furans							
2,3,7,8-TCDD	**X**	**X**	**X**		**X**	**X**	**X**
Total Dioxin/Furan TEQ Fish		**X**	**X**				
Total Dioxin/Furan TEQ Bird					**X**	**X**	
Total Dioxin/Furan TEQ Mammal							**X**
Polychlorinated Biphenyls (PCBs)							
Total PCBs	**X**	**X**	X		**X**	**X**	**X**
Total PCB TEQ Fish		**X**	**X**				
Total PCB TEQ Bird					**X**	**X**	
Total PCB TEQ Mammal							**X**
Total Dioxin/Furan/PCB TEQ Fish		**X**	**X**				
Total Dioxin/Furan/PCB TEQ Bird					**X**	**X**	
Total Dioxin/Furan/PCB TEQ Mammal							**X**
Pesticides							
Total DDx (2,4 & 4,4)	**X**	**X**			**X**	**X**	**X[a]**
Dieldrin	**X**	**X**			**X**	**X[a]**	**X**
Total Chlordane	X[a]	X[a]				X[a]	X[c]
Hexachlorobenzene	X[a]	X[a]				X[a]	X[a]
Polycyclic Aromatic Hydrocarbons (PAHs)							
Total HMW PAH	**X**					X[b]	X[b]
Total LMW PAH	**X**					X[b]	X[b]
Total PAH				X		X	X[d]
Metals/Inorganics							

COPEC	COPECs for the NBSA BERA						
	Benthic Invertebrate Tissue	Fish Tissue	Fish Egg	Fish Diet	Bird Egg	Bird Diet	Mammal Diet
Arsenic	X	X		X[a]		X[a]	X
Cadmium	X			X		X	X
Chromium	X	X[a]		X		X	X[c]
Copper	X[b]	**X[a]**		X		**X**	**X**
Lead	**X**	**X**		X[a]		**X**	**X**
Mercury/Methylmercury	**X**	**X**	**X**	X	**X**	**X**	**X**
Nickel	X			X		X	X
Selenium	X	X		X		X	X
Silver	X	X		X[a]		X[c]	X[c]
Zinc	X	X		X		X	X

Notes:
2,3,7,8-TCDD = tetrachlorodibenzo-*p*-dioxin
BERA = baseline ecological risk assessment
COPEC = constituent of potential ecological concenr
DDD = dichlorodiphenyldichloroethane
DDE = dichlorodiphenyldichloroethylene
DDT = dichlorodiphenyltrichloroethane
HMW = high molecular weight
LMW = low molecular weight
LPR = Lower Passaic River
NBSA = Newark Bay Study Area
PAH = polycyclic aromatic hydrocarbon
PCB = polychlorinated biphenyl
TEQ = toxic equivalency
Total DDx = sum of all six DDT isomers (2,4′-DDD, 4,4′-DDD, 2,4′ DDE, 4,4′-DDE, 2,4′-DDT and 4,4′-DDT)
Bold = COPECs evaluated in the LPRSA BERA and LPR FFS
[a]COPEC not evaluated in LPRSA BERA but TRV available in LPRSA BERA Appendix A3-1 or Appendix E1
[b]COPEC evaluated in LPR FFS but not in the LPRSA BERA
[c]COPEC not evaluated in LPRSA BERA; TRV derived from alternate source
[d] Both the LOAEL and NOAEL TRVs were the same as the LPR FFS TRVs derived for total HMW PAH

Table D-1b Comparison of NBSA and LPR COPECs

Chemical/Chemical Group	NBSA (OU3) BERA COPEC	OU2 LPR FFS COPECs	OU4 LPRSA BERA COPECs
Dioxins/Furans			
2,3,7,8-TCDD	X	X	X
Total Dioxin/Furan TEQ	X	X	X
Polychlorinated Biphenyls (PCBs)			
Total PCBs	X	X	X
Total PCB TEQ	X	X	X
Total Dioxin/Furan/PCB TEQ	X		X
Pesticides			
Total DDx	X	X	X
Dieldrin	X	X	X
Total Chlordane	X		
Hexachlorobenzene	X		
Polycyclic Aromatic Hydrocarbons (PAHs)			
Total HWW PAH	X	X	X
Total LMW PAH	X	X	X
Total PAHs	X		X
Metals/Inorganics			
Arsenic	X		X
Cadmium	X		X
Chromium	X		X
Copper	X	X	X
Lead	X	X	X
Mercury/Methylmercury	X	X	X
Nickel	X		X
Selenium	X		X
Silver	X		X
Zinc	X		X

2 POLYCHLORINATED DIBENZO-*P*-DIOXINS & DIBENZOFURANS

Polychlorinated dibenzo-*p*-dioxins and dibenzofurans are compounds that contain one to eight chlorine atoms attached to the carbon atoms of the parent chemical and are persistent environmental contaminants. They are commonly referred to as dioxins and furans, respectively, and reportedly cause various harmful health and environmental effects (Eisler 2000; Agency for Toxic Substances and Disease Registry [ATSDR] 1994a, 1998). While more than 200 dioxin and furan isomers exist, seven dioxins and 10 furans are known by the World Health Organization (WHO) to be particularly toxic (USEPA 2008a), with the most toxic isomers being 2,3,7,8-TCDD and 2,3,7,8-TCDF. Other dioxin-like chemicals, particularly coplanar polychlorinated biphenyls [PCBs], share structural and biochemical similarities with dioxins and furans as well as a common mode of action through which they exert similar effects on humans and wildlife. Including the coplanar PCBs, there are 29 dioxin-like compounds (17 dioxin and furan congeners and 12 PCB congeners).

In their pure form, dioxins and furans are colorless solids or crystals that enter the environment as mixtures containing a variety of individual components and impurities. In the environment, they tend to be associated with ash, soil, or any media with high organic content. In air and water, a portion of the dioxins and furans may be found in vapor or its dissolved state, depending on the amount of particulate matter, temperature, and other environmental factors (ATSDR 1998).

Dioxins and furans are known to occur naturally but are also produced by human activities. They are naturally produced from the incomplete combustion of organic material by forest fires or volcanic activity. Dioxins and furans are not intentionally manufactured by industry, except in small amounts for research purposes. They are, however, unintentionally produced by industrial, municipal, and domestic incineration and combustion processes. It is believed that dioxin emissions associated with human incineration and combustion activities are the predominant environmental source (ATSDR 1998; USEPA 2006a). Dioxins and furans are released to the environment primarily during combustion of fossil fuels and wood and during incineration processes for municipal and medical solid waste and hazardous waste (ATSDR 1994a, 1998). Dioxins are also produced in the manufacture of chlorinated chemicals, such as chlorophenols, chlorobenzenes, and chlorobiphenyl (USEPA 2006a). Additionally, dioxins have been detected at low concentrations in cigarette smoke, home-heating systems, and car exhaust. Burning materials that may contain chlorine, such as plastics, wood treated with pentachlorophenol (PCP), pesticide-treated wastes, other polychlorinated chemicals (e.g., PCBs), and bleached paper, can produce dioxins and furans (ATSDR 1998).

In aquatic environments, due to their hydrophobic nature, the majority of dioxins and furans ultimately become associated with the organic fraction of suspended and/or bed sediments and the lipid-rich tissues of aquatic organisms (Wenning et al. 2011; Saloranta et al. 2006; USEPA 1998a; Hoffman et al. 1995). Dioxins and furans have been shown to bioaccumulate via the ingestion of dioxin- and furan-laden food items and soil/sediment particles and are primarily eliminated slowly through digestion and egg production. Field studies and models have shown that fish body burdens of dioxins and furans are largely due to dietary rather than gill surface uptake (Saloranta et al. 2006; Micheletti et al. 2008). Concentrations of dioxins and furans (particularly tetra- and penta-chlorinated dibenzo-*p*-dioxins and tetra- and penta

chlorinated dibenzofurans) tend to be highest in top predator species in food webs wherein successive stages of dietary accumulation at each trophic level result in significant biomagnification (Khairy et al. 2014; Wenning et al. 2011; Saloranta et al. 2006; Micheletti et al. 2008).

In order to more readily assess the toxicity of dioxins and furans as a mixture, the system of toxicity equivalency factors (TEFs) was developed based on the toxicity of 2,3,7,8-TCDD. In this system, each isomer on the WHO list is assigned a factor (i.e., TEF) based on its potency relative to 2,3,7,8-TCDD; the estimated toxicity of all isomers present is summed to come up with an overall estimate of toxicity, called the 2,3,7,8-TCDD toxic equivalency (TEQ). These TEFs have been developed for ecological risk assessment of fish, birds, and mammals, as described in USEPA (2008a) and Van den Berg et al. (1998).

Toxicity for these compounds is thought to be broken into three modes of action: 1) irreversible chemical binding to macromolecules inhibiting their function, 2) accumulating to high concentrations in lipids resulting in stress-induced dosing, and 3) irreversible binding to cellular receptors and enzymes inhibiting biochemical communications between cells (USEPA 2008a; Eisler 2000; Van den Berg et al. 1998; Hoffman et al. 1995). Most, if not all, toxic effects of dioxins and furans are initiated by activation of the cellular aryl hydrocarbon receptor (AhR), a ligand-activated transcription factor that is involved in the regulation of biological responses to planar aromatic hydrocarbons (e.g., dioxins, furans, PCBs, and polycyclic aromatic hydrocarbons [PAHs]) (Farmahin et al. 2013). The AhR is involved in regulating xenobiotic-metabolizing enzymes, such as cytochrome p450.

Invertebrate and vertebrate organisms respond differently to elevated concentrations of dioxins and furans, with invertebrates being relatively tolerant of exposure compared to vertebrate species. This difference may be due to the absence of some receptors in invertebrates that are adversely affected in vertebrate species (Eisler 2000; Hoffman et al. 1995). Due to their tolerance to exposure, invertebrates may accumulate dioxins and furans into their tissues from sediments, making them more biologically available to vertebrate species in the aquatic environment (Eisler 2000; Hoffman et al.1995).

Laboratory toxicity data show that fish are generally more sensitive to 2,3,7,8-TCDD than plants, aquatic invertebrates, and other aquatic vertebrates (e.g., amphibians) (USEPA 2008a; Eisler 2000). The high lipid content in fish makes them highly susceptible to bioaccumulation of 2,3,7,8-TCDD in their tissues, which can essentially be transferred into the food web to higher-trophic-level organisms, such as birds and mammals (including humans). Effects of 2,3,7,8-TCDD exposure to mammals and birds are similar to fish and include delayed mortality, a “wasting” syndrome characterized by reduced food intake and reduced body weight, reproductive toxicity, histopathological alterations, developmental abnormalities, and immunosuppression (USEPA 2008a; Eisler 2000). More specific ecotoxicological information is provided below by receptor group.

2.1 Benthic Invertebrates

2.1.1 Toxicity Profile

Benthic invertebrates lack an AhR receptor and, as such, are not considered to be sensitive to the cellular mediated effects of these compounds like vertebrate organisms. However, invertebrates accumulate these compounds and thus create a potential exposure risk for organisms that consume these receptors. There is a great deal of uncertainty regarding the potential effects of dioxins/furans on invertebrates, and

the scientific literature on effects is relatively sparse and variable, compared to vertebrate organisms (Eisler 2000). The toxic effects of 2,3,7,8-TCDD exposure on the eastern oyster (*Crassostrea virginica*) have been studied by Cooper and Wintermyer (2009). Similarly, the toxic effects of dioxin exposure on crabs have been reported by Weis et al. (2011) and Reichmuth et al. (2010); both of these studies evaluated behavior endpoints.

2.1.2 TRVs

Table D-2 summarizes the benthic invertebrate TRVs used in the assessment, and the sections below describe how they were derived.

Table D-2 Benthic Invertebrate 2,3,7,8-TCDD TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	0.0003	0.003	Ashley et al. 1996	1	a,b
		0.00000015	0.0000013	Wintermyer and Cooper 2003 (eastern oyster reproduction)	2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10
ww = wet weight

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

Ashley et al. (1996) is the only study identified that reported a 2,3,7,8-TCDD TRV for crustaceans. A LOAEL of 0.003 milligram per kilogram (mg/kg) wet weight (ww) was reported for the survival of crayfish; a 25% mortality was observed after a 45-day exposure via cephalothoracic injection. No NOAEL was identified from this study. A NOAEL of 0.0003 mg/kg was estimated from the LOAEL using an extrapolation factor of 10. Several uncertainites are associated with these TRVs: mortality is generally not the most sensitive endpoint based on chemical exposure, tissue concentrations were not reported, the test individuals were wild-caught, and only 3 or 4 individuals were exposed per treatment. However, it is a reported TRV for a crustacean species, and the derivation of the NOAEL was conservative to account for the uncertainties.

The LPR FFS (USEPA 2014) derived a LOAEL TRV of 0.0000013 mg/kg ww and a NOAEL TRV of 0.00000015 mg/kg ww based on a 10-month field study of adult eastern oysters transplanted to two locations in New Jersey (Wintermyer and Cooper 2003). The results from one location (Arthur Kill), where 23 percent (%) fertilization success occurred, became the LOAEL and the results from the other location (Sandy Hook), where 54% fertilization success occurred, became the NOAEL. There are several uncertainties with this study: reported tissue concentrations were based on one composite of seven oysters from each site, the endpoint, fertilized egg development was based on one sample, the presence

of other contaminants were not considered or evaluated, and a true control group was not used for comparison. The application of this oyster TRV to blue crab is uncertain given the cross-taxanomic extrapolation, but provides for a bounding of risk estimates, given the lack of available TRVs for blue crab or crustaceans for non-survival endpoints.

2.2 Fish

2.2.1 Toxicity Profile

Dioxins and furans have been reported to generate a broad range of toxic effects in fish under controlled exposure conditions, including reduced survival, body weight loss, edema, hemorrhaging, craniofacial malformations, toxemia, and reproductive and developmental effects (Eisler 2000; Elonen et al. 1998; Fisk et al. 1997; Spehar et al. 1997; Tietge et al. 1998). Although toxicological sensitivity is species specific, teleost fish tend to be more sensitive to dioxins and furans than most other vertebrates (Walker and Peterson 1994). Recently, cardiovascular and other developmental impacts (such as swim bladder effects) in fish embryos from sublethal exposure to dioxin have been studied (Aluru et al. 2015; Chen 2015; Yue et al. 2015; Park et al. 2014). In addition, behavioral effects have been observed in fish as a result of exposure to dioxins/furans and related compounds (e.g., PCBs and PAHs) (Weis et al. 2011). While fish are sensitive to low dose exposures of dioxins and furans, Salomon (1994) showed that most dietary exposure is not absorbed by the gastrointestinal tract but rather most is eliminated in the feces.

2.2.2 TRVs

Table D-3 summarizes the fish TRVs used in the assessment, and the sections below describe how they were derived.

Table D-3 Fish 2,3,7,8-TCDD and Total TEQ[1] TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	0.000012	0.00012	Windward 2019 (7 species SSD);	1	a,b
		0.00000089	0.0000018	Couillard et al. 2011 (mummichog behavior)	2	c
Fish whole-body tissue; Alternative TRV)	mg/kg ww	0.0000023	0.000023	Windward 2019 (7 species SSD)	1	a,b
Fish egg	mg/kg ww	0.0000072	0.000086	Steevens et al. 2005 (10 species; growth, survival, reproduction, and behavior)	1, 2	a

Notes:
[1] = Total TEQ refers to total dioxin/furan TEQ, total PCB TEQ, and total PCB and dioxin/furan/PCB TEQ.
KU = Key Uncertainty
a = TRV based on a species sensitivity distribution (SSD)
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10
c = TRV based on a single study

Table D-3 Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

2.2.2.1 Fish Whole-Body Tissue

The NOAEL and LOAEL TRVs of 0.000012 and 0.00012 mg/kg ww, respectively, for 2,3,7,8-TCDD and TEQ derived in the LPRSA BERA (Windward 2019) were based on an SSD developed from nine studies and seven fish species where the LOAELs for the adverse effects on reproduction, growth, or survival ranged from 0.000085 to 0.014 mg/kg ww. The selected LOAEL represents the geometric mean 5th percentile LOAEL of the SSD models evaluated (i.e., the Pearson6, log-logistic, and Weibull distributions). The NOAEL TRV (0.000012 mg/kg ww) was extrapolated from the LOAEL TRV using an uncertainty factor of 10. There is uncertainty associated with the derivation of a NOAEL based on an extrapolation factor.,

The LPRSA BERA also derived an alternative TRV for whole body fish tissue using the same dataset. A 5th percentile LOAEL (0.000023 mg/kg ww) based on the beta general distribution was selected as a conservative TRV. The NOAEL was estimated using an uncertainty factor of 10.

The LPR FFS (USEPA 2014) LOAEL and NOAEL of 0.0000018 and 0.00000089 mg/kg ww, respectively, for 2,3,7,8-TCDD and TEQ were also used as TRVs and are based on reported impacts on prey capture behavior in newly hatched mummichogs following topical exposure of the eggs to PCB 126 at doses of 50 kilograms per liter (kg/L) (Couillard et al. 2011). Larvae tissue concentrations were estimated from empirical data on the ratio of larval tissue concentration to topical dose measured in a previous study (Couillard et al. 2008). The estimated larval tissue concentrations (0.000355 and 0.000178 mg/kg ww) were converted to estimated TEQ concentrations by multiplying the fish toxic equivalency factor (TEF) for PCB 126 (0.005), resulting in the LOAEL and NOAEL of 0.0000018 and 0.00000089 mg/kg ww, respectively. There are several uncertainties associated with these LPR FFS (USEPA 2014) TRVs: 1) this study is more relevant to the fish egg assessment than adult fish; 2) the assessment endpoints of growth, reproduction, and survival showed no adverse effects, even at the highest doses; 3) relating a study on the toxicity of one PCB congener (126) to the toxicity of a sum of toxic dioxin congeners and dioxin-like PCBs; and 4) concentrations in mummichog larvae were not measured in the same study that recorded impacts on behavior. The larval tissue concentrations were estimated from data in another study that provided a ratio of larval tissue concentration to topical, and this ratio was based on one data point (Couillard et al. 2008, 2011). These extrapolated TRVs in fish larvae are also an order of magnitude lower than the measured TRVs for fish eggs from multiple species described below, indicating a large degree of uncertainty with the derivation/use of this TRV.

2.2.2.2 Fish Eggs

Steevens et al. (2005) developed an SSD for 2,3,7,8-TCDD based toxicity studies on 10 species of early life stage fish. The 5th percentile upper confidence limit (UCL) and lower confidence limit (LCL) values of 0.000086 and 0.0000072 mg/kg ww, respectively, from this SSD were selected as the fish eggs TRVs for dioxins/furans and TEQ. These TRVs were used in both the LPRSA BERA (Windward 2019) and in the LPR FFS (USEPA 2014).

2.3 Birds

2.3.1 Toxicity Profile

In birds, dioxins and furans have been reported to produce various effects under controlled exposure conditions. Some effects in laboratory testing have included mortality, body weight loss, effects on egg production and hatchability, and embryo survival (Eisler 2000; Hoffman et al. 1998; Powell et al. 1998; Powell et al. 1997; Janz and Bellward 1996; Nosek et al. 1992a, 1992b; Schwetz et al. 1973)). For wild birds in aquatic habitats, reported effects included increased embryo and hatchling mortality, teratogenicity, reduced growth, edema, alternations in thyroid function, hepatic porphyria, and increased hepatic retinoid levels (Janz and Bellward 1996). Bird species' sensitivity to dioxin-like compounds varies more than 1,000-fold in association with differences in the structural characteristics of the AhR (Farmahin et al. 2013; Cohen-Barnhouse et al. 2011; Head et al. 2008). Eighty-six bird species have been grouped into three classes of sensitivity to dioxin-like compounds: 1) high sensitivity; 2) moderate sensitivity; and 3) low sensitivity (Farmahin et al. 2013). Chickens (*Gallus domesticus*) have demonstrated to be among the most sensitive species. The spotted sandpiper (a Lower Passaic River Study Area [LPRSA]-focal species) is in the moderate sensitivity group, and the belted kingfisher (*Megaceryle alcyon*) and great blue heron (also LPRSA-focal species) are in the low sensitivity group. While causation is difficult to establish, because local populations of birds are exposed to mixtures of chemicals, area-specific studies on immunotoxicity and adverse reproductive effects based on exposure to PCBs (and dioxins) have been conducted (Grasman et al. 2012).

2.3.2 TRVs

Table D-4 summarizes the bird TRVs used in the assessment, and the sections below describe how they were derived.

Table D-4 Bird 2,3,7,8-TCDD and TEQ[1] TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	0.000014	0.00014	Nosek et al. 1992a (ring-necked pheasant [*Phasianus colchicus*] mortality, growth, and reproduction)	1	a
		0.0000028	0.000028		2	a
Bird egg	mg/kg ww	0.000025	0.00025	Windward 2019 (five species reproduction)	1	b, c
		0.000059	0.00015	USEPA 2003 (multiple species, including chicken reproduction)	2	b

Notes:
[1] = Total TEQ refers to total dioxin/furan TEQ, total polychlorinated biphenyl (PCB) TEQ, and total PCB and dioxin/furan TEQ.
KU = Key Uncertainty
a = TRV based on a single study
b = TRV based on an SSD
c = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Table D-4 Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

2.3.2.1 Bird Diet

The selected TRVs were derived in the LPRSA BERA (Windward 2019). Toxicity data were limited for the dietary effects of dioxins/furans and dioxin-like PCBs on birds. Only two studies were found acceptable for evaluation of the 2,3,7,8-TCDD TRV—one study on ring-necked pheasants exposed by intra-peritoneal injection (Nosek et al. 1992a) and the second study on chickens exposed by oral intubation (Schwetz et al. 1973). The ring-necked pheasant study had the lowest LOAEL of 0.000143 mg/kg body weight (bw)/day (Nosek et al. 1992a) and was based on a 57% increase in mortality observed 16 weeks after the initiation of 10 weeks of weekly injections of 2,3,7,8-TCDD. No mortality was observed at the NOAEL of 0.0000143 mg/kg bw/day. The LOAEL and NOAEL from Nosek et al. (1992a) were selected as the TRVs. These study endpoints were also the basis for TRVs in the FSS (USEPA 2014); however, the LPR FFS applied a species sensitivity factor of 5 to derive recommended TRVs on the basis that ring-necked pheasants were not among the most sensitive species.

2.3.2.2 Bird Eggs

The selected TRVs were derived in the LPRSA BERA (Windward 2019), which developed an SSD based on five acceptable egg injection studies evaluating 2,3,7,8-TCDD toxicity. These studies reported the embryo survival and hatchability for five bird species with LOAELs that ranged from 0.001 to 0.04 mg/kg ww 2,3,7,8-TCDD. The 5th percentile of the LOAELs was determined to be 0.00025 mg/kg ww, which was accepted as the LOAEL TRV. This SSD-derived LOAEL represents a conservatively extrapolated value that is less than the study LOAELs on which the SSD was based. The highest NOAEL TRV was estimated from the LOAEL using a factor of 10.

The LPR FFS (USEPA 2014) also used the 5th percentile of an SSD as the LOAEL TRV, but it included chickens while the LPRSA SSD did not (USEPA 2003). Given the known high sensitivity of the chicken to dioxins/furans relative to other bird species (Farmahin et al. 2013), it is not surprising that the derived LOAEL TRV of 0.00015 mg/kg ww was lower than the LOAEL TRV derived without chicken data. The NOAEL TRV of 0.000059 mg/kg ww was also derived from USEPA guidance (2003) for SSDs.

2.4 Mammals

2.4.1 Toxicity Profile

As with PCBs (see Section 3.4.1 below), the most comprehensive studies of dioxin/furan toxicity in a non-domesticated mammal have been conducted with mink (*Neovison vison*), which has been shown to be highly sensitive to dioxins. In mink, dioxins and furans have been shown, under controlled exposure conditions, to have adverse effects on reproduction (e.g., fertility, litter size, and offspring survival). These effects are comparable to those caused by PCBs (Hochstein et al. 2001). Similar effects have been reported in less sensitive mammals, such as guinea pigs [*Cavia porcellus*] and rats [Rattus], and there is evidence that dioxins and furans also have adverse impacts on developmental toxicity, hepatotoxicity, endocrine disruption, immunotoxicity, adult mortality, and body weight (Eisler 2000; Hochstein et al. 1998;

Kennedy et al. 1996; Van Birgelen et al. 1994). Studies evaluating the toxicity of 2,3,7,8-TCDD to mammals (i.e., guinea pigs, rats, or mink) have reported adverse effects on growth, reproduction, and survival following exposure to dietary 2,3,7,8-TCDD (Kociba et al. 1978; Murray et al. 1979; DeCaprio et al. 1986; Van Birgelen et al. 1994; Hochstein et al. 2001).

2.4.2 TRVs

Table D-5 summarizes the mammal TRVs used in the assessment, and the sections below describe how they were derived.

Table D-5 Mammal 2,3,7,8-TCDD and TEQ[1] TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	0.0000026	0.0000088	Hochstein et al. 2001 (mink reproduction)	1	a
		0.00000008	0.0000022	Tillitt et al. 1996 (mink reproduction)	2	a

Notes:
[1] = Total TEQ refers to total dioxin/furan TEQ, total PCB TEQ, and total PCB and dioxin/furan TEQ.
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

The selected TRVs were derived in the LPRSA BERA (Windward 2019), which reviewed six laboratory toxicity studies testing three species (mink, guinea pig, and rat) with mammals exposed to 2,3,7,8-TCDD incorporated into their diet. The guinea pig was found to have the lowest LOAEL (0.0000049 mg/kg bw/day). The second lowest LOAEL (0.0000088 mg/kg bw/day), however, was selected as the TRV because the test species (mink) was better related to the mammalian receptor of interest (river otter). The mink LOAEL resulted in decreased kit survival at 3 and 6 weeks after birth compared to the control (Hochstein et al. 2001). The selected NOAEL TRV of 0.0000026 mg/kg bw/day came from the same study.

The LPR FFS (USEPA 2014) LOAEL and NOAEL of 0.0000022 and 0.00000008 mg/kg bw/day, respectively, were developed from a study feeding mink field-collected contaminated carp (Tillett et al. 1996). The toxicity study by Tillitt et al. (1996) is preferred for evaluating ecological risks specific to the region where the study was conducted (Saginaw Bay, Michigan); however, it is less preferred than a laboratory study when characterizing the potential for toxicity of 2,3,7,8-TCDD in other systems because of the number of unique aspects of the ecosystem that can affect toxicity: multiple contaminants, heterogeneous genetic composition, contaminant bioavailability, and non-contaminant potential stressors such as disease, weather, and food availability. For the NBSA, site-specific field toxicity studies are not available, and the extent to which the contaminant mixture evaluated by Tillitt et al. (1996) is representative of the contaminant mixture in the NBSA is uncertain. Exposure to dioxins, furans, dioxin-

like PCBs in the NBSA BERA was evaluated using the 2,3,7,8-TCDD TEQ approach, in which concentrations of individual constituents are adjusted based on relative toxicity to a 2,3,7,8-TCDD. Therefore, use of the TRVs based on only 2,3,7,8-TCDD (Hochstein et al. 2001) is more appropriate for use with the TEQ approach used in the NBSA BERA, and the Hochstein et al. (2001) TRVs are considered to produce risk estimates with lower uncertainty than the Tillitt et al. (1996) TRVs. While site-specific field studies such as Tillitt et al. (1996) are preferred over laboratory studies for evaluating toxicity of a particular site, and can provide information useful for bounding risk estimates, they are not generally preferred over laboratory studies at different sites because of the great inherent number of variables that can influence the toxicity between sites.

3 POLYCHLORINATED BIPHENYLS

The PCBs are a group of synthetic organic chemicals that can cause a number of harmful effects. PCBs are either oily liquids or solids and range from colorless to light yellow in appearance, with no known taste or odor. Some PCBs are volatile and may exist as a vapor in air. There are no known natural sources of these persistent bioaccumulative contaminants in the environment. PCBs enter the environment as mixtures containing a variety of individual chlorinated biphenyl components, known as congeners, as well as impurities. PCBs do not burn easily, are good insulating materials, and have been previously widely used as coolants and lubricants in transformers, capacitors, and other electrical equipment. The manufacture of PCBs stopped in the United States in 1977 because of evidence that PCBs persist in the environment and possibly cause harmful effects (ATSDR 2000).

Because the health effects of environmental mixtures of PCBs are difficult to evaluate, most of the available toxicological information pertains to seven types of PCB mixtures (i.e., Aroclors 1016, 1221, 1232, 1242, 1248, 1254, and 1260) that were commercially produced. These mixtures include 35% of all PCBs commercially produced and 98% of all PCBs sold in the United States since 1970 (ATSDR 2000). The potency of PCB mixtures depends on chlorine content. In general, mixtures with higher chlorine content (i.e., Aroclors 1242, 1248, 1254, and 1260) are more toxic than mixtures with lower chlorine content (i.e., Aroclors 1221 and 1232).

Coplanar PCBs have chlorine atoms in non-ortho positions that allow the two benzene rings to lie in the same plane; non-coplanar PCBs have chlorine atoms in the ortho position causing the molecule to twist and the rings are on different planes. The relative toxicities of coplanar PCBs are calculated as TEQ by expressing their TEFs in relation to 2,3,7,8-TCDD, as described in Section 2. Toxicity of PCBs is a factor of both the number of chlorine atoms in the molecule and how close the benzene rings are to being coplanar (USEPA 2008a).

PCB toxicity varies among different species of animals, but in general, reproductive effects tend to be the most sensitive endpoint. PCBs may also act as endocrine disruptors. Toxicity is believed to be related to the ability of the congeners to induce cytochrome P450 dependent activity (ATSDR 2000).

There are limited data regarding toxicity of PCBs to plant species. PCBs incorporated into phytoplankton exert inhibitory effects on photosynthesis and cell motility (Eisler 2000). PCB toxicity to invertebrates is generally less than that observed in vertebrate species due to limited detoxification systems. Crustaceans and younger developmental stages appear to be the most sensitive groups, and lower chlorinated compounds appeared to be more toxic.

In aquatic environments, due to their hydrophobic nature, PCBs ultimately become associated with the organic fraction of suspended and/or bed sediments and the lipid-rich tissues of aquatic organisms (USEPA 2008a; Eisler 2000; Hoffman et al. 1995). PCBs have been shown to bioaccumulate via the ingestion of PCB-laden food items and soil/sediment particles and are primarily eliminated slowly through digestion and egg production.

PCB effects may be associated with the survival, growth, and reproduction of individuals within the local populations of fish and wildlife species, with reproduction broadly defined to include egg maturation, spawning, egg hatchability, and survival of fish larvae. The most sensitive endpoint for effects of PCB on fish is found during early life stage survival and recruitment as a result of PCB transfer from maternal tissue to eggs (Eisler 2000). As a group, birds are more resistant to acutely toxic effects of PCBs than

mammals, based on literature values (Eisler 2000. Signs of PCB poisoning among birds included morbidity, tremors, beak pointed upwards, and muscular incoordination (Eisler 2000). In mammals, long-term neurobehavioral changes were reported in children, monkeys, and rodents exposed to commercial PCB mixtures during fetal and neonatal development (Eisler 2000). Mink is among the most sensitive mammals to PCB toxicity (USEPA 2008a), with documented reproductive failure, fetal death, altered blood chemistry, abnormal liver metabolism and histology, raised cortisol excretion, and altered metabolism of Vitamin A (Eisler 2000). More specific ecotoxicity information is provided below by receptor group.

3.1 Benthic Invertebrates

3.1.1 Toxicity Profile

Once in the environment, most PCBs are known to bioaccumulate into the food web in aquatic environments, although lower chlorinated PCBs may not bioaccumulate (Khairy et al. 2014). Adverse ecotoxicological effects of PCBs on various aquatic invertebrates, including eastern oysters, sea urchins (*Arbacia punctulata*), grass shrimp (*Palaemonetes pugio*), pink shrimp (*Penaeus duorarum*), and blue crabs, have been observed and include decreased shell growth (USEPA 1980c; Ernst 1984), reduced fertilization success (Adams 1983), reduced reproductive success (Chu et al. 2000; Chu et al. 2003), and increased mortality (Hansen et al. 1974; Duke et al. 1970; Nimmo et al. 1974).

3.1.2 TRVs

Table D-6 summarizes the benthic invertebrate TRVs used in the assessment, and the sections below describe how they were derived.

Table D-6. Benthic Invertebrate PCB TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	0.052	0.52	(Windward 2019) (10 species SSD)	1	a, b
		0.0064	0.017	Chu et al. 2000; Chu et al. 2003 (eastern oyster reproduction)	2	c

Notes:
KU = Key Uncertainty
a = TRV based on an SSD
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10
c = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)2 = LPR FFS (USEPA 2014)

Nine studies with 10 invertebrate species that examined the growth, reproduction, and mortality endpoints of PCBs were available to derived PCB TRVs for invertebrates. Windward (2019) derived an SSD that plotted 11 chronic and 5 acute-to-chronic ratio (ACR) derived LOAELs ranging from 0.13 to 552 mg/kg ww. The 5th percentile of the SSD (0.52 mg/kg ww) was selected as the LOAEL TRV. This calculated LOAEL is less than the available LOAELs from the individual studies on which the SSD was based; therefore, it represents a conservative estimate of potential toxicity. The NOAEL was estimated from the LOAEL using an extrapolation factor of 10.

Chu et al. (2000) exposed eastern oysters for 30 days to an algal diet contaminated with PCB Aroclors and measured total PCB accumulation within the oysters. The later study, Chu et al. (2003), examined PCB accumulation and adverse reproductive effects measured by the number of spawned oysters after 76 days of exposure to 0.35 microgram per liter (µg/L), and no-adverse-effect on reproduction after 30 days of exposure to 0.10 µg/L PCBs (Chu et al. 2003). An extrapolated LOAEL egg tissue concentration of 52 micrograms per kilogram (µg/kg) ww was derived for the exposure of 0.35 µg/L using a regression based on the exposure concentrations (0.1 and 1 µg/L) and egg tissue concentrations (0.020 and 0.134 mg/kg ww) reported by Chu et al. (2000). The egg tissue LOAEL and NOAEL of 0.052 and 0.02 mg/kg ww, respectively, were converted to an adult tissue LOAEL and NOAEL of 0.017 and 0.0064 mg/kg ww, respectively, using the adult:egg lipid ratio of 0.25:0.08 (Windward 2019). There are three main uncertainties associated with the selected TRVs: 1) a no dose-responsive relationship was observed among the females that had spawned (Chu et al. 2003); 2) no PCB analysis was conducted on eggs, and the authors believed that PCB concentrations in the 2003 study might have exceeded those found in 2000 (Chu et al. 2003); and 3) the two studies used different doses and exposure conditions and assumed a linear relationship between dose and egg tissue.

3.2 Fish

3.2.1 Toxicity Profile

Adverse effects on fish reported in toxicological studies for 14 fish species (i.e., Atlantic croaker [*Micropogonias undulatus*], Atlantic salmon [*Salmo salar*], brook trout [*Salvelinus fontinalis*], channel catfish [*Ictalurus punctatus*], Chinook salmon [*Oncorhynchus tshawytscha*], coho salmon [*Oncorhynchus kisutch*], common barbel [*Barbus barbus*], fathead minnow [*Pimephales promelas*], goldfish [*Carassius auratus*], mummichog, pinfish [*Lagodon rhomboides*], rainbow trout [*Oncorhynchus mykiss*], sheepshead minnow [*Cyprinodon variegatus*], and spot [*Leiostomus xanthurus*]) include reduced body weight; mortality; reduced early life stage or fry growth and survival; and reduced fecundity, hatchability, and spawning success following exposure to PCBs via diet, water, or maternal transfer to eggs (Bengtsson 1980; DeFoe et al. 1978; Fisher et al. 1994; Freeman and Idler 1975; Hansen et al. 1971; 1974a; 1974b; 1975; Hattula and Karlog 1972; Hendricks et al. 1981; Hugla and Thome 1999; Lieb et al. 1974; Matta et al. 2001; Mauck et al. 1978; Mayer et al. 1977; Mayer et al. 1985; McCarthy et al. 2003; Nebeker et al. 1974; Powell et al. 2003; van Wezel et al. 1995). Recently, behavioral effects have also been observed in fish as a result of exposure to PCBs (and dioxins and PAHs) (Weis et al. 2011).

3.2.2 TRVs

Table D-7 summarizes the fish TRVs used in the assessment, and the sections below describe how they were derived.

Table D-7 Fish PCB TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	0.38	3.8	Windward 2019 (11 species SSD)	1	a, b
		0.17	0.53	Lerner et al. 2007 (Atlantic salmon smolt behavior)	2	c
Fish egg	mg/kg ww	0.0258	0.258	Hugla and Thome 1999 (common barbel reproduction)	1	c, b

Notes:
KU = Key Uncertainty
a = TRV based on an SSD
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10
c = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

3.2.2.1 Fish Whole-Body Tissue

The NOAEL and LOAEL TRVs of 0.38 and 3.8 mg/kg ww, respectively, for total PCB derived in the LPRSA BERA (Windward 2019) were based on an SSD developed from 12 studies and 11 fish species where the LOAELs for the adverse effects on growth or survival ranged from 9.3 to 645 mg/kg ww. The selected LOAEL represents the 5th percentile of the SSD. The NOAEL TRV (0.000012 mg/kg ww) was extrapolated from the LOAEL TRV using an uncertainty factor of 10. There is uncertainty associated with the derivation of a NOAEL based on an extrapolation factor.

The LPR FFS (USEPA 2014) LOAEL and NOAEL TRVs for fish based on a study of Atlantic salmon smolt aqueously exposed as eggs and an endpoint of behavioral change, a substantial decrease in volitional preference for seawater (Lerner et al. 2007). The LOAEL and NOAEL TRVs are 0.53 and 0.17 mg/kg ww tissue.

3.2.2.2 Fish Eggs

The selected TRVs were derived in the LPRSA BERA (Windward 2019) where aliterature search yielded four egg LOAELs for four species (Atlantic croaker, brook trout, rainbow trout, and common barbel), which ranged from 0.258 to 77.9 mg/kg in eggs. The lowest LOAEL of 0.258 mg/kg ww was selected as the TRV and represents reduced hatchability in common barbels fed 12.5 mg/kg PCBs for 75 days. The NOAEL TRV was estimated from the LOAEL using an extrapolation factor of 10. Fish egg TRVs for PCBs were not developed in the LPR FFS (USEPA 2014).

3.3 Birds

3.3.1 Toxicity Profile

Effects on birds from exposure to dietary PCBs include disruption of normal patterns of growth, reproduction, metabolism, and behavior. The most sensitive effects are related to reproduction, and include egg production, fertility, and hatching success (Eisler 2000). Of the bird species used to examine reproductive endpoints in laboratory studies, chickens and other galliformes, such as ring-necked pheasant and quail (*Coturnix coturnix*), have been found to be the most sensitive to PCB toxicity (Kennedy et al. 1996). In other studies that evaluated the toxicity of PCBs to various wild bird species (e.g., American kestrels [*Falco sparverius*], Japanese quails [*Coturnix japonica*], mallard ducks [*Anas platyrhynchos*], screech owls [*Megascops asio*], and turtle doves [*Streptopelia turtur*]), adverse effects were observed on reproductive endpoints (e.g., fertility, hatchability, eggshell thickness, egg production, eggshell weight, embryo development, clutch size, and embryo mortality and viability) following dietary exposure to PCBs (Lowe and Stendell 1991; McLane and Hughes 1980; Hill et al. 1976a; Peakall et al. 1972; Peakall and Peakall 1973; Custer and Heinz 1980; Risebrough and Anderson 1975; Fernie et al. 2000; Fernie et al. 2001; Fernie et al. 2003a; Fernie et al. 2003b; Fernie et al. 2003c; Haseltine and Prouty 1980). While causation is difficult to establish because local populations of birds are exposed to mixtures of chemicals, area-specific studies on immunotoxicity and adverse reproductive effects based on exposure to PCBs (and dioxins) have been conducted (Grasman et al. 2012).

3.3.2 TRVs

Table D-8 summarizes the bird TRVs used in the assessment, and the sections below describe how they were derived.

Table D-8 Bird PCB TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	0.14	1.4	Peakall et al. 1972; Peakall and Peakall 1973 (ringed turtle-dove [*Streptopelia risoria*] reproduction)	1	a
		0.4	0.5	Chapman 2003 (chicken reproduction)	2	b
Bird egg	mg/kg ww	1.6	16	Peakall et al. 1972; Peakall and Peakall 1973 (ringed turtle-dove reproduction)	1	a
		0.7	1.3	Chapman 2003 (chicken reproduction)	2	b

Notes:
KU = Key Uncertainty
a = NOAEL estimated from a LOAEL with an extrapolation factor of 10
b = TRV based on a single study

Table D-8 Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

3.3.2.1 Bird Diet

The selected TRVs were derived in the LPRSA BERA (Windward 2019). Although there were 11 bird studies, excluding chickens, on the adverse effects (all reproductive) of dietary PCBs, Windward data were insufficient to develop an SSD because effects were only reported for four bird species. The lowest LOAEL from these studies was 1.4 mg/kg bw/day, based on reduced hatching success in ringed turtle-dove (Peakall et al. 1972; Peakall and Peakall 1973). No NOAEL was reported in the study with ringed turtle-doves, so an uncertainty factor of 10 was applied to the LOAEL for a NOAEL TRV of 0.14 mg/kg bw/day.

The LPR FFS (USEPA 2014) used a chicken study as the basis of the TRVs while the LPRSA BERA (Windward 2019) avoided studies with domestic chickens because they have been shown to be in the most highly sensitive category of all birds tested with dioxin-like compounds including PCBs (Farmahin et al. 2013). In addition, because domesticated species are bred to have high egg-laying rates compared to wild bird species, TRVs based on domestic reproductive endpoints are uncertain. These LPR FFS (USEPA 2014) TRVs, a LOAEL and NOAEL of 0.5 and 0.4 mg/kg bw/day, respectively, were also used in this study to bound the risk estimates. These TRVs were based on an interpolated 10% decrease hatchability relative to control (the NOAEL) and an interpolated 25% hatchability decrease relative to control (the LOAEL) as described by Chapman (2003) and based on data reported by Scott (1977). The study by Scott (1977) examined chicken hatchability effects after 8 weeks of exposure to Aroclor 1248. It is not known whether an effect threshold of 25% reduction in chicken egg hatchability is predictive of potential population-level effects in wild birds.

3.3.2.2 Bird Eggs

The same studies used to derive the bird diet TRVs (Peakall et al. 1972; Peakall and Peakall 1973;, Chapman 2003) were also used as the basis for the egg TRVs.

3.4 Mammals

3.4.1 Toxicity Profile

PCBs have been reported to elicit a broad range of toxic effects in laboratory mammals under controlled exposure conditions, including lethality, hepatotoxicity, porphyria, body weight loss, dermal toxicity, thymic atrophy, immunosuppressive effects, reproductive and developmental effects, carcinogenesis, and neurotoxicity (Eisler 2000; Seegal 1996; Battershill 1994; Delzell et al. 1994; Safe 1994; Bolger 1993; WHO 1993; Silberhorn et al. 1990; Kimbrough 1987). In general, the gastrointestinal tract of most mammals readily absorbs PCBs, but the absorption rate may be affected by the dose level and lipophilicity of the compound (Eisler 2000; Van den Berg et al. 1998). There is evidence to support the placental transfer of PCBs in mammals (Eisler 2000), and PCBs can also accumulate in the lipid portion of milk, resulting in exposure of suckling young.

Fertility, litter size, and offspring survival appear to be among the most sensitive in vivo endpoints of PCB toxicity in mammals (Golub et al. 1991; Rice and O'Keefe 1995; Hoffman et al. 1996). Reproductive success can be affected directly by toxic action on the differentiated reproductive tract, or indirectly by toxic action on systems that regulate reproduction (e.g., endocrine and central nervous systems). In laboratory studies, PCBs have been reported to elicit a broad range of direct and indirect effects associated with reproductive functions. Direct effects on the gonads and the female reproductive tract have been reported (Fuller and Hobson 1986). The precise mechanism by which PCBs cause reproductive effects in mammals remains unclear, but reproductive success appears to be a sensitive integrated endpoint of in vivo toxicity.

The most comprehensive studies of PCB toxicity in a non-domesticated mammal have been conducted with mink. Mink also appear to be one of the most sensitive mammalian species tested (Fuller and Hobson 1986), and therefore, are often used as a surrogate for the assessment of risk to other mammals. In studies that evaluated the toxicity to mink of dietary exposure to PCBs, adverse effects on maternal growth, kit growth, kit survival, whelping success, and reproductive success were reported for captive-bred mink (Aulerich and Ringer 1977; Jensen et al. 1977; Ringer 1983; Aulerich et al. 1985; Wren et al. 1987; Brunström et al. 2001; Chapman 2003).

3.4.2 TRVs

Table D-9 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-9 Mammal PCB TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	0.08	0.096	Chapman 2003 (mink; reproduction)	1	a
		0.069	0.082		2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

The selected TRVs were derived for the LPRSA BERA (Windward 2019) in which 14 toxicity studies were available and reviewed for the derivation of total PCB TRV for mammals and included 12 studies with mink and two studies conducted with mice (*Mus musculus*). There were not enough species to derive an SSD (Windward 2019). Mink are known to be sensitive to PCBs. Five of the 14 studies reviewed used dietary exposures to field-collected fish that could have other contaminants besides PCBs in their tissues and thus could interfere with the derivation of a TRV specific to PCBs. Chapman (2003) evaluated mink PCB toxicity data to derive TRVs for USEPA Region 5 based on interpolation of laboratory toxicity data

from Aulerich and Ringer (1977), Wren et al. (1987), and Kakela (2002)—none of which used field-collected fish.

The interpolated dietary concentration, resulting in a 25% decrease in endpoint response (1.1 µg/kg ww), was determined to be the low-effect level for Aroclor 1254, and the interpolated dietary concentration associated with a 10% decrease in endpoint response (1.0 mg/kg ww) was determined to be the no-effect level (Chapman 2003). A factor of 0.52 was applied to the LOAEL and NOAEL to account for the lower effect levels observed in several studies that were conducted over 2 years or into the second generation (Brunström et al. 2001, Restum et al.1998), resulting in adjusted interpolated dietary concentrations of 0.6 and 0.5 mg/kg ww, respectively. These concentrations in food were converted to dietary LOAEL and NOAEL doses of 0.096 and 0.080 mg/kg bw/day, respectively, assuming a female food ingestion rate (FIR) of 0.16 mg/kg bw/day from Bleavins and Aulerich (1981).

The LPR FFS (USEPA 2014) LOAEL and NOAEL of 0.082 and 0.069 mg/kg bw/day, respectively, were also selected for total PCBs based on the same interpolated effect levels reported by Chapman (2003) but are slightly different because of the different FIR (0.137 kilogram per day [kg/day]) used to convert these food doses to dietary doses.

Because both of these sets of TRVs were derived from the same study, mammal risk endpoint thresholds from an alternate study (Bursian et al. 2013) were compared; although, these were not used quantitatively as a third set of TRVs in this assessment to remain consistent with the LPRSA mammal risk assessment. As requested by theUSEPA, the study evaluated as part of this uncertainty analyses was the mink PCB-feeding study (Bursian et al. 2013), which was included in the risk assessment for the Hudson River (USEPA 2019). In this study, a dietary concentration of 0.34 part per million (ppm) PCBs in food fed to adult mink resulted in 20% mortality (LC20) of 6-week old kits born to those mink. The dietary LC20 (0.34 ppm PCBs) is that concentration in the diet which will result in 20% kit mortality (LC20) at six weeks of age. The LOAEL TRV derived from this study is 0.033 mg/kg-BW/day, approximately three times lower than the TRVs used for the NBSA. From this LOAEL, a factor of three was applied to estimate a NOAEL of 0.11, which is approximately seven times lower than the NOAEL used for the NBSA. A key uncertainty with the use of this assessment for the NBSA is that the fish fed to the mink were from the Hudson River, which means that the fish contain other contaminants and concentrations of these that are specific to the Hudson River and this inherently makes them not appropriate for use for the NBSA. Instead, this assessment could be added to the SSD, which was the basis of the NBSA TRVs because studies that used wild caught fish as food were included. The effect of adding this study would be to lower the 5th percentile of the SSD that was used as the LOAEL, but this LOAEL would not be as low as the Bursian et al. (2013) LOAEL itself.

4 ORGANOCHLORINE PESTICIDES – TOTAL DDX

Dichlorodiphenyltrichloroethane (DDT) is an anthropogenic organochlorine pesticide. Total DDx refers to the sum of all six DDT isomers that are the result of metabolism or degradation of DDT (i.e., 2, 4′-dichlorodiphenyldichloroethane [DDD], 4,4′-DDD, 2,4′-dichlorodiphenyldichloroethylene [DDE], 4,4′-DDE, 2,4′-DDT, and 4,4′-DDT).

The commercial use of DDT began in 1939. It was primarily applied to agricultural crops but was also used in forests and residential properties. The United States banned the use of DDT in 1972, but it is still used in other parts of the world to control disease-bearing vectors, such as mosquitoes (ATSDR 2002b). Prior to 1975, DDT was a widely used pesticide in the United States and primarily entered the environment through its application to agricultural lands. Upon entering the environment, DDT can partition into air, soil/sediment, and water. DDT and its related compounds can be subject to global distillation in air by atmospheric transport from warmer to colder climates. As a result, DDT and its associated derivatives are commonly found in areas far away from the original application.

Following introduction via the gills or through ingestion of prey items, organochlorines including DDT travel through the blood and are then distributed to soft organs and ultimately lipids (USEPA 1999). DDT and its related compounds are persistent and bioaccumulative. Its deposition and subsequent association with soil particles can leave a persistent footprint, but it can also be metabolized by microorganisms within the soil. In aquatic systems, DDT is most often associated with suspended particles and sediment, from where it can enter the aquatic food web and bioaccumulate and biomagnify at higher trophic levels (ATSDR 2002b; Eisler 2000). While toxic to invertebrates and vertebrates alike, the most severe effects of DDx are on higher-order predators such as piscivorous birds and mammals, where eggshell thinning and reproductive failure can occur (Eisler 2000). More specific ecotoxicity information is provided below by receptor group.

4.1 Benthic Invertebrates

4.1.1 Toxicity Profile

DDT and its metabolite, DDE, are highly persistent and lipophilic compounds that are subject to pronounced biomagnification. DDE is very persistent in aquatic systems, absorbing strongly to sediments and bioconcentrating in aquatic organisms. DDE tends to bioconcentrate in lower-trophic levels and will accumulate in food webs. DDE will bioconcentrate in freshwater and marine plankton, insects, mollusks, and other invertebrates (Eisler 2000; Oliver and Niimi 1985).

Several studies have examined the adverse effects of DDT on various aquatic invertebrates. These studies observed adverse effects on reproduction, survival, and growth. Increased mortality as a result of DDT exposure was observed in studies of pink shrimp (Nimmo et al. 1970), the amphipod (*Hyallela azteca*) (Landrum et al. 2005), and the water flea (*Daphnia magna*) (Crosby and Tucker 1971). Reduced offspring production was observed in a study of the amphipod (*Leptocheirus plumulosus*) exposed to DDT (Lotufo et al. 2001). Decreased growth was observed in studies of the polychaete worm (*Armandia brevis*) exposed to DDT (Rice et al. 2000).

4.1.2 TRVs

Table D-10 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-10 Benthic Invertebrate Total DDx[1] TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	0.011	0.11	Windward 2019 (6 species SSD)	1	a, b
Benthic invertebrate whole-body tissue; Alternative TRV	mg/kg ww	0.001	0.01	Windward 2019 (6 species SSD)	1	a, b
Benthic invertebrate whole-body tissue	mg/kg ww	0.06	0.13	Nimmo et al. 1970 (pink shrimp mortality)	2	c

Notes:
[1] = DDx refers to all isomers of DDT (2,2',4, and 4') and well as the isomers of metabolites of DDT (DDE and DDD).
KU = Key Uncertainty
a = NOAEL estimated from a LOAEL with an extrapolation factor of 10
b = TRV based on an SSD
c = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

The LPRSA BERA (Windward 2019) developed an SSD based on eight studies examining mortality, growth, and reproductive endpoints. Eleven LOAELs ranging from 0.13 to 266 mg/kg ww were identified for six species. The 5th percentile of the SSD based on a gamma distribution was selected as the LOAEL TRV (0.11 mg/kg ww). The NOAEL TRV (0.011 µg/kg ww) was extrapolated from the LOAEL TRV using an uncertainty factor of 10. There is uncertainty associated with the derivation of a NOAEL based on an extrapolation factor.

The LPRSA BERA also derived an alternative TRV for benthic invertebrate tissue using the same dataset. A 5th percentile of the SSD based on a beta general distribution was selected as a conservative LOAEL (0.01 mg/kg ww) TRV. The NOAEL was estimated using an uncertainty factor of 10.

The LPR FFS (USEPA 2014) developed both the LOAEL and NOAEL TRVs of 0.13 and 0.06 mg/kg ww from a study of pink shrimp exposed to aqueous DDx compounds for 56 days (Nimmo et al. 1970). The LOAEL was based on the body burdens of pink shrimp that had died at day 28 of the experiment, and the NOAEL concentration represents where no mortality occurred. An uncertainty of the study noted by the authors was that "stress related to laboratory confinement was probably responsible for a portion of the

mortalities;" however, the degree to which this impacted the TRV cannot be quantified (Nimmo et al. 1970).

4.2 Fish

4.2.1 Toxicity Profile

Several studies have been conducted to examine the adverse toxicological effects on various fish species (sailfin molly [*Poecilia latipinna*], fathead minnow, goldfish, and several salmonid species) as a result of exposure to DDTs (Allison et al. 1964; Benton et al. 1994; Macek 1968a; Jarvinen et al. 1977; Rhead and Perkins 1984; Buhler et al. 1969). These studies observed adverse effects on reproduction, survival, and growth. Increased mortality as a result of DDT exposure was observed in studies of coho and Chinook salmon, goldfish, and fathead minnow (Allison et al. 1964; Allison et al. 1963; Buhler et al. 1969; Jarvinen et al. 1976). Decreased growth was observed in studies of sailfin molly exposed to DDT (Benton et al. 1994). Embryo mortality of yearling brook trout chronically exposed to DDT was observed by Macek (1968b).

4.2.2 TRVs

Table D-11 summarizes the fish TRVs used in the assessment, and the section below describes how they were derived.

Table D-11 Fish Total DDx[1] TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	0.052	0.52	Windward 2019 (7 species SSD)	1	a, b
		0.078	0.39	Beckvar et al. 2005 (9 species SSD)	2	a

Notes:
[1] = DDx refers to all isomers of DDT (2,2',4, and 4') and well as the isomers of metabolites of DDT (DDE and DDD).
KU = Key Uncertainty
a = TRV based on an SSD
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Source:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

The NOAEL and LOAEL TRVs of 0.52 and 0.052 mg/kg ww, respectively, for total DDx derived in the LPRSA BERA (Windward 2019) were based on an SSD developed from six studies and seven fish species where the LOAELs for the adverse effects on reproduction or survival ranged from 1.1 to 200 mg/kg ww. The selected LOAEL represents the 5th percentile of the SSD. The NOAEL TRV (0.052 mg/kg ww) was extrapolated from the LOAEL TRV using an uncertainty factor of 10. There is uncertainty associated with the derivation of a NOAEL based on an extrapolation factor.

The LPR FFS (USEPA 2014) also developed a LOAEL TRV (0.39 mg/kg ww) based on the 5th percentile of an SSD (Beckvar et al. 2005) and the 10 LOAELs for 9 species of fish used in the SSD came from USACE's ERED database. LOAELs ranged from 0.29 to 112.7 mg/kg ww for survival, growth, reproduction, and behavior endpoints. The lowest LOAEL was from Berlin et al. (1981), where lake trout (*Salvelinus namaycush*) survival was adversely affected; however, the test fish came from eggs field-collected from Lake Michigan which also had high concentrations of PCBs, total DDx, and mercury. The next two higher LOAELs: 0.55 mg/kg ww from Butler (1969) and 1.65 mg/kg ww from Davy et al. (1972) also had conditions that make the results unreliable. In Butler (1969), pinfish (*Lagodon rhomboides*) survival was not tissue concentration dependent. The endpoint from Davy et al. (1972) was altered locomotor activity in goldfish and was not correlated to the more relevant endpoints of survival, growth, or reproduction.

4.3 Birds

4.3.1 Toxicity Profile

Historically, the use of DDT resulted in population declines of wild raptors, including bald eagle (*Haliaeetus leucocephalus*), peregrine falcon (*Falco peregrinus*), and osprey (*Pandion haliaetus*), which highlighted the adverse effects that DDT-related compounds have on bird reproduction. Laboratory studies conducted on barn owl (*Tyto alba*), American kestrel, mallard duck, black duck (*Anas rubripes*), Japanese quail, bobwhite quail (*Colinus virginianus*), and ringed turtle-doves verified field observations of adverse effects, including decreased eggshell thickness and duckling weight, increased mortality, reduced offspring survival, and reduced fertility and hatchability (Eisler 2000; Mendenhall et al. 1983; Peakall et al. 1973; Heath et al. 1969; Longcore et al. 1971; Longcore and Samson 1973; Kolaja 1977; Davison and Sell 1974; Shellenberger 1978).

One hypothesized mechanism of action to explain these effects is that a DDT derivative inhibits the prostaglandin synthesis in the shell glad mucosa, reducing the ability of the glad to deposit calcium carbonate onto the developing eggshell that, in turn, causes a reduction in eggshell thickness and a decline in reproductive success (ATSDR 2002b). Lundholm (1987) described the mode of action of DDE on calcium regulation in birds, which contributes to eggshell thickness. Maternal transfer of DDT to pheasant and ringed turtle-dove chicks is also associated with reduced post-hatch survival as a result of direct toxicity (Haegele and Hudson 1973; Genelly and Rudd 1956).

4.3.2 TRVs

Table D-12 summarizes the bird TRVs used in the assessment, and the sections below describe how they were derived.

Table D-12 Bird Total DDx[1] TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	0.025	0.25	Windward 2019 (10 species SSD)	1	a, b
		0.009	0.027	Anderson et al. 1975 (brown pelican [*Pelecanus occidentalis*]; reproduction)	2	c, d
Bird egg	mg/kg ww	0.41	4.1	Windward 2019 (seven species SSD)	1	a, b
		0.5	3.0	Blus 1984 (brown pelican; reproduction)	2	c

Notes:
[1] = DDx refers to all isomers of DDT (2,2',4, and 4') and well as the isomers of metabolites of DDT (DDE and DDD).
KU = Key Uncertainty
a = TRV based on an SSD
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10
c = TRV based on a single study
d = NOAEL estimated from a LOAEL with an extrapolation factor of 3

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

4.3.2.1 Bird Diet

The NOAEL and LOAEL TRVs of 0.25 and 0.025 mg/kg bw/day, respectively, for total DDx derived in the LPRSA BERA (Windward 2019) were based on an SSD developed from 20 studies on the effects of DDx in bird diets were available and reviewed for the development of a bird dietary TRV for DDx. The LOAELs for 10 species based on eggshell thickness, adult survival, offspring survival, or hatchability, ranged from 0.15 to 71.1 mg/kg bw/day. The LOAEL TRV of 0.25 mg/kg bw/day represents the 5th percentile of the SSD. No NOAEL below the selected LOAEL TRV could be identified, so the NOAEL (0.025 mg/kg bw/day) was derived from the LOAEL TRV by a factor of 10. There is uncertainty associated with the derivation of a NOAEL based on an extrapolation factor.

The LPR FFS (USEPA 2014) developed LOAEL and NOAEL TRVs of 0.027 and 0.0009 mg /kg bw/day, respectively, for total DDx based on brown pelican reproduction data from Anderson et al. (1975). The LOAEL TRV of 0.027 mg/kg bw/day was based on observations about productivity and eggshell thinning compared to standards known to support a stable population (Anderson et al. 1975). An extrapolation factor of three was used to derive the NOAEL TRV from the LOAEL. Uncertainties of this study are: 1) the significance of changes in eggshell thinning and productivity was not analyzed; 2) a critical threshold level was devived by association to the concentration at which productivity had improved but not recovered relative to historical levels; and 3) the impacts may have resulted from exposure to multiple chemicals in the fish diet, although DDE was the only contaminant directly linked to eggshell thinning in birds (Anderson et al. 1975).

4.3.2.2 Bird Eggs

Windward (2019) developed an SSD from eight acceptable toxicity studies on bird egg tissue, DDx effect levels with LOAELs for eggshell thickness, embryo and offspring survival, and hatchability reported for seven bird species. The LOAELs from these studies ranged from 12 to 658 mg/kg ww and the selected LOAEL TRV (4.1 mg/kg ww) represents the 5th percentile of the SSD and was lower than the lowest LOAEL of 12 mg/kg ww for nestling mortality in barn owls (Mendenhall et al. 1983). The NOAEL TRV (0.41 mg /kg ww) was estimated from the LOAEL using an extrapolation factor of 10.

LOAEL and NOAEL TRVs of 3.0 and 0.5 mg/kg ww, respectively, developed in the LPR FFS (USEPA 2014) were selected for total DDx based on the study by Blus (1984). The LOAEL TRV, 3.0 mg/kg ww, represents the concentration at which there was 50% nesting success in the brown pelican. The NOAEL TRV (0.5 mg/kg ww) was derived from the same study and was estimated as the median concentration between non-detected concentrations to 1.0 mg/kg where within this range nesting success was 30%. The fact that these TRVs were based on a field study introduces the uncertainties that other stresses (e.g., chemical or non-chemical) could potentially have also influenced reproductive success.

4.4 Mammals

4.4.1 Toxicity Profile

Adverse effects from total DDx exposure of mammals in toxicological studies have been observed in mice, rats, and hamsters (Cricetinae) (Eisler 2000). Observed adverse effects in rats included reduced litter sizes, offspring weights, survival of young, viable litter size, adult survival, and body weight (Duby et al. 1971; Ottoboni 1972; Fitzhugh 1948; Jonsson et al. 1976; Banerjee et al. 1996). Similarly, studies examining adverse effects on mice from exposure to DDT and related compounds noted reduced litter sizes, adult survival, male growth, lifespan, and survival of young (Cannon and Holcomb 1968; Tomatis et al. 1974; Turusov et al. 1973; Shabad et al. 1973; Ware and Good 1967). In addition, reductions in survival and body weight were observed in hamsters after exposure to DDT, and adverse reproductive effects were observed in dogs (*Canis lupus familiaris*) after exposure to DDT (Rossi et al. 1983; Ottoboni et al. 1977).

4.4.2 TRVs

Table D-13 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-13 Mammal Total DDx[1] TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	0.13	1.3	Ware and Good 1967 (mouse reproduction)	1,3	a, b
		0.8	4.0	Fitzhugh 1948 (rat reproduction)	2	a

Table D-13 Notes:

[1] = DDx refers to all isomers of DDT (2,2',4, and 4') and well as the isomers of metabolites of DDT (DDE and DDD).

KU = Key Uncertainty

a = TRV based on a single study

b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Table D-13 Sources:

1 = TRV derived for the NBSA BERA

2 = LPR FFS (USEPA 2014)

3 = LPRSA BERA (Windward 2019); Appendix A3-1

Dietary TRVs for DDT were not assessed in the LPRSA BERA (Windward 2019), but were available from Appendix A3-1 the LPR FFS (USEPA 2014). The NBSA LOAEL TRV of 1.3 mg/kg bw/day was based on a study of the effects of DDT on mouse reproduction (Ware and Good 1967) where the specific endpoint of reduced litter size in mice fed a DDT mixture during a critical life stage (gestation) over 120 days. A chronic NOAEL was extrapolated from the chronic LOAEL using an extrapolation factor of 10.

The LPR FFS (USEPA 2014) TRVs were developed from a long-term reproduction study that evaluated multi-generational toxicity and sensitive endpoints in Sprague-Dawley rats (*Rattus norvegicus domesticus*) (Fitzhugh 1948). The selected LOAEL and NOAEL TRVs are 0.8 and 4.0 mg/kg bw/day, respectively, and are based on reproductive success.

There is not another line of evidence to evaluate the magnitude of difference in the TRVs developed by the NBSA BERA and the LPR FFS (USEPA 2014).

5 ORGANOCHLORINE PESTICIDES – DIELDRIN

Dieldrin is a white, powdery substance that was applied to agricultural soils and around residential and commercial buildings as an insecticide beginning in the 1950s. Its application to agricultural crops, such as corn and cotton, was halted in 1970, but the use of dieldrin to kill termites continued from 1972 to 1987. Dieldrin is no longer manufactured or used as an insecticide in an agricultural or commercial setting (ATSDR 2002a). Aldin (an insecticide similar to dieldrin) generally degrades into dieldrin both in the body and in the environment, thus dieldrin can also be found in areas where aldrin was used (ATSDR 2002a).

Dieldrin is nonpolar and lipophilic, so upon entering the environment, it sorbs to soil particles where it remains immobile and will not leach into groundwater. In aquatic environments, dieldrin sorbs to sediment and soil particulates, from where it can be transported in surface waters. It does not readily degrade in water or soil. Dieldrin can be taken up by plant tissues and is known to bioaccumulate in aquatic food webs, where it is stored in lipid tissues (ATSDR 2002a; Eisler 2000). More specific ecotoxicity information is provided below by receptor group.

5.1 Benthic Invertebrates

5.1.1 Toxicity Profile

Dieldrin, like DDT, is on an organochlorine pesticide with a high molecular weight and has been shown to be eliminated from invertebrates slower than other compounds (e.g., endosulfan), as demonstrated in the polychaete (*Nereis virens*) (Haya and Burridge 1988) and clam (*Macoma nasuta*) (Boese et al. 1997). The potential for accumulation of dieldrin and transfer up the food chain is a principle attribute of concern. Beckvar and Lotufo (2011) found lethal critical body residues in the range of 0.08 to 2.1 mg/kg ww based on four species of invertebrates species, including pink shrimp, grass shrimp, midge (*Chironomus riparius*), and ostracod (*Chlamydotheca arcuate*), with pink shrimp being the most sensitive. Adverse effects on growth rates were observed in eastern oyster exposed to dieldrin (Parrish et al. 1973; Parrish et al. 1974) and reduced fecundity was observed in quahog clams (*Mercenaria mercenaria*) and mud snails (*Nassa obsoleta*) exposed to dieldrin (Eisler 1970).

5.1.2 TRVs

Table D-14 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-14 Benthic Invertebrate Dieldrin TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	0.008	0.08	Parrish et al. 1973 (pink shrimp survival)	1	a,b
		0.0016	0.008		2	b

Notes:
KU = Key Uncertainty
a = NOAEL estimated from a LOAEL with an extrapolation factor of 10
b = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

The LPRSA BERA derived TRVs from a study of pink shrimp mortality by Parrish et al. (1973). In this study, the concentration of 0.08 mg/kg ww was associated with 25% mortality after 96 hours of exposure to dieldrin in water. Whole-body tissues of pink shrimp with 0% mortality were below detection limits (< 0.01 mg/kg ww); therefore, a NOAEL of 0.008 mg/kg ww was derived from the LOAEL using an extrapolation factor of 10. There is uncertainty associated with the derivation of a NOAEL based on an extrapolation factor.

The LPR FFS (USEPA 2014) used the same study, Parrish et al. (1973), as the basis of TRVs, but applied an ACR of 10 to the LOAEL because it was an acute exposure and was extrapolated to a chronic effect. Thus, a LOAEL TRV of 0.008 mg/kg ww was developed. The NOAEL TRV of 0.0016 mg/kg ww was based on the tissue residues reported in the control group (0.016 mg/kg ww) divided by an ACR of 10.

5.2 Fish

5.2.1 Toxicity Profile

Adverse effects, including decreased growth and survival, have been reported in toxicological studies for multiple species of fish (Eisler 2000). Gakstatter and Weiss (1967) observed that bluegill (*Lepomis macrochirus*) exposed to dieldrin experienced equilibrium loss and convulsions and reported that goldfish exposed to dieldrin experienced hyper-excitability. Although these effects are not a direct measure of survival, they could impair the organism's ability to avoid predation. Studies examining adverse effects from exposure to dieldrin in largemouth bass (*Micropterus salmoides*) and rainbow trout observed reductions in body weight, length, and survival (Muller et al. 2004; Poels et al. 1980).

5.2.2 TRVs

Table D-15 summarizes the fish TRVs used in the assessment, and the section below describes how they were derived.

Table D-15 Fish Dieldrin TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	0.12	0.2	Shubat and Curtis 1986 (rainbow trout survival)	1	a
		0.008	0.04		2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

Two studies with two species examining effect following dieldrin exposure were available and evaluated to develop the fish tissue TRV for dieldrin. The LOAEL TRV is the lower of the two LOAELs and was obtained from the study by Shubat and Curtis (1986). This study reported reduced growth of rainbow trout following exposure to aqueous dieldrin for 16 weeks with an associated average tissue burden of 0.2 µg/kg ww. The NOAEL TRV comes from the same study, where no adverse effects on growth were observed in fish at the next lower aqueous exposure level associated with a tissue burden of 0.12 µg/kg ww.

The LPR FFS (USEPA 2014) TRVs were also developed from the same study (Shubat and Curtis 1986), but the TRVs derived by the LPR FFS were different for two reasons: 1) they assumed the reported concentrations were expressed on a dry weight basis, and 2) they applied an uncertainty factor of two in the estimation of the NOAEL to estimate chronic effect levels from the subchronic study.

5.3 Birds

5.3.1 Toxicity Profile

Adverse effects, including decreased growth, reproduction, and survival, were reported in toxicological studies for six bird species (Japanese quail, bobwhite quail, ring-necked pheasant, chicken, mallard duck, and American robin [*Turdus migratorius*]) exposed to dieldrin. Observed effects include reductions in egg production, hatchability, eggshell thickness, clutch size fertility, body weight, offspring survival, and adult survival (Eisler 2000; DeWitt 1956).

5.3.2 TRVs

Table D-16 summarizes the bird TRVs used in the assessment, and the sections below describe how they were derived.

Table D-16 Bird Dieldrin TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	0.08	0.12	De Witt 1956 (quail reproduction and mortality)	1,3	a
		0.054	0.18	Wiese et al. 1968 (helmeted guinea fowl [*Numida meleagris*] survival)	2	a
Bird egg	mg/kg ww	0.3	3	Genelly and Rudd 1956 (pheasant reproduction)	1	a, b
		0.2	8.1	Mendenhall et al. 1983 (barn owl reproduction)	2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Sources:
1 = TRV derived for the NBSA BERA
2 = LPR FFS (USEPA 2014)
3 = LPRSA BERA (Windward 2019) Appendix A3-1

5.3.2.1 Bird Diet

The LPRSA BERA (Windward 2019) did not evaluate bird dietary TRVs, but they were available from the LPRSA BERA Appendix A3-1. The LOAEL and NOAEL TRVs of 0.12 and 0.08 mg/kg bw/day, respectively, come from a study by DeWitt (1956). In this study, Japanese quail were exposed to dieldrin in the diet for 5 months and a 17% mortality was observed at the LOAEL TRV concentration (0.12 mg.kg bw/day). The LPR FFS-derived LOAEL and NOAEL TRV values selected are the lowest relevant bounded study results presented in the USEPA Ecological Soil Screening Level (Eco SSL) document for avifauna (USEPA 2005c). In this study, Wiese et al. (1968) exposed helmeted guinea fowl to seven levels of dieldrin in the diet of female birds for 21 months and identified significant survival effects at the LOAEL concentration of 0.18 mg/kg bw/day.

5.3.2.2 Bird Eggs

The selected TRVs were derived in the LPRSA BERA (Windward 2019) where of the three studies evaluated, the LOAEL TRV of 3 mg/kg ww for dieldrin was selected based on ring-neck pheasant reproduction (Genelly and Rudd 1956). None of the three acceptable studies reported a NOAEL. The NOAEL TRV was derived from the LOAEL TRV using an extrapolation factor of 10. An uncertainty associated with the TRVs is that another study on pheasant reproduction reported a LOAEL an order of magnitude higher (33.6 mg/kg ww).

LPR FFS (USEPA 2014) LOAEL and NOAEL TRVs of 8.1 and 0.2 mg/kg ww, respectively, were also selected for dieldrin based on values reported by Mendenhall et al. (1983) for barn owl reproductive

success. Eggs with concentrations of 8.1 mg/kg ww were reported to have eggshell thickness reduced by 5.5%; however, there was no reduction in breeding success. Thus, the potential for adverse effects on wildlife populations is uncertain. The NOAEL TRV comes from the NOAEL of 0.2 mg/kg ww from the same study and represents the control concentration.

5.4 Mammals

5.4.1 Toxicity Profile

Studies examining exposure to dieldrin in mammals (mouse and rat) via dietary uptake found adverse effects on reproduction, survival, growth, and behavior (Eisler 2000). Dietary exposures to dieldrin in these studies ranged from 120 days to 3 generations. Effects reported in these studies included a decrease number of conceptions, litter size, body weight, pup survival, tendency, and anti-predator response, and an increased onset of nursing (Bildstein and Forsyth 1979; Harr et al. 1970; Treon and Cleveland 1955; Good and Ware 1969; Virgo and Bellward 1977; Fitzhugh et al. 1964).

5.4.2 TRVs

Table D-17 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-17 Mammal Dieldrin TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	0.015	0.03	Harr et al. 1970 (rat reproduction)	1, 2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

Eight toxicity studies were available from the literature in which mammals were exposed to dietary dieldrin, but Windward (2019) determined that they were not sufficient to derive an SSD. The LOAEL TRV of 0.03 mg/kg bw/day represents the lowest LOAEL and resulted in adverse reproductive effects in rats (Harr et al. 1970). The NOAEL from this study of 0.015 mg/kg bw/day was also used as the basis for the NOAEL TRV. These are the same TRVs that were used in the LPR FFS (USEPA 2014). This study was also cited in USEPA's Eco SSL document for dieldrin (USEPA 2005c), making the credibility of these data more reliable.

6 ORGANOCHLORINE PESTICIDES – TOTAL CHLORDANE

Chlordane is a chemical belonging to the class of chlorinated pesticides. It was used as a pesticide in the United States from 1948 to 1988 when it was administered to crops, lawns, and gardens primarily as a termite control (ATSDR 1994a). Although it is no longer used in the United States, it is still produced and exported for use in other countries. Technical chlordane was a mixture of several pesticides, including alpha-chlordane, gamma-chlordane, heptachlor epoxide, oxychlordane, heptachlor endo-epoxide, trans-nonachlor, and cis-nonachlor. Total chlordane includes cis- and trans-isomers of chlordane that, once ingested, can be metabolized and form metabolic products, such as heptachlor and heptachlor epoxide, which can be more toxic than the parent compound. The dominant form of chlordane in tissues is trans-nonachlor and cis-chlordane (Eisler 2000). In this BERA, these compounds are summed to establish a total chlordane concentration in sediment and biota tissue samples for evaluation of potential risks. Therefore, the TRVs discussed in this section are applicable to the sum of these compounds.

Chlordane is toxic to freshwater invertebrates and fish. It is also known to bioaccumulate in both marine and freshwater aquatic fish and, subsequently, to be biomagnified up the food web to higher trophic-level consumers (ATSDR 1994a). Reported effects in aquatic organisms include a reduction in survival, immobilization, impaired reproduction, and histopathology (Eisler 2000). Chlordane is reportedly carcinogenic to wildlife, and also can cause adverse effects on the central nervous system and liver (Eisler 2000; ATSDR 1994a). It is also a mutagen in mammalian cell systems and has been shown to cause reproductive effects in animals (ATSDR 1994a). More specific ecotoxicity information is provided below by receptor group.

6.1 Benthic Invertebrates

6.1.1 Toxicity Profile

There is less toxicity data for chlordane than dieldrin, which is similar in structure, also a cyclodiene, but has demonstrated to be lower in molecular weight, residence time, and toxicity. Chlordane toxicity has been evaluated in brown shrimp, grass shrimp, eastern oyster, blue crab, water fleas, amphipods, and polychaetes. Reported effects include decreased shell growth (Mayer 1987; Parrish et al. 1976), overt signs of stress (McLeese et al.1982), increased mortality (Parrish et al. 1976), and immobilization (Mayer 1987; Cardwell et al. 1977; Passino and Smith 1987). Beckvar and Lotufo (2011) indicated that lethal critical body residues in pink and grass shrimp range from 1.7 to 9.1 mg/kg ww, respectively.

6.1.2 TRVs

Table D-18 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-18 Benthic Invertebrate Total Chlordane TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	0.71	1.7	Parrish et al. 1976 (pink shrimp mortality)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Source:
1 = TRV derived for the NBSA BERA

Total chlordane was not a COPEC evaluated in either the LPRSA BERA (Windward 2019) or the LPR FFS (USEPA 2014). TRVs for total chlordane were available in the LPRSA BERA Appendix A3-1. Of the three studies that met acceptability criteria, the study by Parrish et al. (1976) had the lowest LOAEL (1.7 mg/kg ww) and NOAEL (0.71 mg/kg) and were accepted as TRVs. The LOAEL represents 55% mortality of marine pink shrimp (*Penaeus duorarum*) after 96 hours of water exposures and the NOAEL represents 10% mortality. Pink shrimp were the most sensitive invertebrate of those studied by Parrish et al. (1976) where the other species tested were eastern oysers (*Crassostrea virginica*) and grass shrimp (*Palaemonetes pugio*).

6.2 Fish

6.2.1 Toxicity Profile

Chlordane toxicity to fish varies and is dependent on the exposure to and uptake of the component compounds being evaluated in different studies. Adverse effects of chlordane exposure in fish species, including sheepshead minnow, freshwater catfish (*Heteropneustes fossilis*), and goldfish, include reduced hatching rate (Parrish et al. 1978), increased mortality (Parrish et al. 1978; Moore et al. 1977), loss of equilibrium (Parrish et al. 1976), loss in fry (Parrish et al. 1976), and muscle glycogenolysis and hyperglycemia (Mishra and Srivastava 1984). Chlordane lethal critical body residues in fish were reported by Beckvar and Lotufo (2011) for two species: 0.71 mg/kg for mortality in whole-body spot and 11.1 mg/kg for mortality in whole-body sheepshead minnow.

6.2.2 TRVs

Table D-19 summarizes the fish TRVs used in the assessment, and the section below describe how they were derived.

Table D-19 Fish Chlordane TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	1.66	16.6	Parrish et al. 1976 (pinfish mortality)	1,2	a

Table D-19 Notes:
KU = Key Uncertainty
a = TRV based on a single study

Table D-19 Sources:
1 = TRV derived for the NBSA BERA
2 = LPRSA BERA (Windward 2019) Appendix A3-1

Total chlordane was not a COPEC evaluated in either the LPRSA BERA (Windward 2019) or the LPR FFS (USEPA 2014); however, TRVs for total chlordane were available in the LPRSA BERA Appendix A3-1. This LOAEL TRV of 16.6 mg/kg bw/day is based on a study of juvenile pinfish mortality after a 96-hr exposure to aqueous chlordane by Parrish et al. (1976). The LOAEL represents a 30% mortality. A NOAEL was derived using a factor of 10 applied to the LOAEL. There are several uncertainties with the use of this LOAEL TRV: 1) the study was short-term, and 2) the mortality endpoint is typically not as sensitive as sublethal endpoints. Windward

6.3 Birds

6.3.1 Toxicity Profile

Based on the affinity of chlordane to accumulate in lipids, bird tissues with high lipid content have been shown to accumulate the highest levels of chlordane. In general, older birds and raptors also tend to accumulate higher levels, but chlordane isomers occur frequently in birds collected nationwide (Eisler 2000). Regarding the persistence in bird tissues of various chlordane compounds, Elliott et al. (1988) found oxychlordane to be the most persistent (half-life of 35.4 years), followed by cis-nonachlor (half-life of 19.4 years), and cis-chlordane (half-life of 11.2 years) in northern gannets (*Sula bassana*). Oxychlordane is a metabolite of chlordane that in birds is more toxic and persistent than chlordane (Kawano et al. 1988).

Observed effects of chlordane toxicity in birds included sluggishness, drooped eyelids, fluffed feathers, low crouching on perch, reduced food intake, quivering and panting rapidly, and convulsing (Stickel et al. 1983). Adverse effects could be observed within 5 minutes of exposure, and death usually occurred within 8 days (Eisler 2000). Adverse effects in birds, including blue-winged teals (*Anas discors*), northern shovelers (*Anas clypeata*), American coots (*Fulica americana*), red-winged blackbirds (*Agelaius phoeniceus*), mallard ducks, Japanese quails, ring-necked pheasants, and bobwhite quails include increased mortality (Hill et al. 1975; Heath et al. 1972), reduced growth rates (Ludke 1976), reduced reproduction (National Research Council of Canada [NRCC] 1975) and reduced food consumption (Hill and Camardese 1986). Lundholm (1988) demonstrated with two species of ducks (*Anas* spp.) and the domestic chicken that various organochlorine compounds, including chlordane, interfered (in a dose-dependent manner) with reproduction by reducing the binding of progesterone to its cytoplasmic receptor in the shell gland mucosa of birds, especially ducks. Sensitive species noted by Eisler (2000) included: California quail (*Callipepla californica*), ring-necked pheasant, and European starlings (*Sturnus vulgaris*).

6.3.2 TRVs

Table D-20 summarizes the bird TRV used in the assessment, and the section below describes how it was derived.

Table D-20 Bird Chlordane TRVs

Tissue	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	2	20	Hill et al. 1975 and Heath et al. 1972 (bobwhite mortality)	1,2	a, b

Notes:
KU = Key Uncertainty
a = TRV based on two studies
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Source:
1 = TRV derived for the NBSA BERA
2 = LPRSA BERA (Windward 2019) Appendix A3-1

Total chlordane was not a COPEC evaluated in either the LPRSA BERA (Windward 2019) or the LPR FFS (USEPA 2014); however, TRVs for total chlordane were available in the LPRSA BERA Appendix A3-1. The LOAEL TRV of 20 mg/kg bw/day is based on toxicity studies by Hill et al. (1975) and Heath et al. (1972) for mortality in bobwhite quail after 5 days of exposure. The main uncertainties with the use of this LOAEL TRV are that the study was short-term and that the mortality endpoint is typically not as sensitive as sublethal endpoints.

Bird egg residues for total chlordane from which TRVs could be developed were not found during a literature search. Therefore, because it is unknown, chlordane bird egg tissue residues did not have risk quantified.

6.4 Mammals

6.4.1 Toxicity Profile

Evidence of total chlordane biomagnification has been shown in aquatic mammals and, particularly, marine mammals (Eisler 2000). Chlordane concentrations in marine mammals were positively related to lipid content but not to the animal age (Perttila et al. 1986). Many signs and symptoms can accompany acute toxicity of chlordane in mammals, some of which include, in addition to death: irritability, salivation, labored respiration, muscle tremors, incoordination, convulsions, pulmonary congestion, degenerative changes in the central nervous system, and avoidance of food and water (Eisler 2000). Exposure to chlordane induced liver cancer in domestic mice (WHO 1984; Tojo et al. 1986) and thyroid neoplasms and malignant fibrous histocytomas in rats (Ohno et al. 1986). Chlordane exposure through diet adversely affected growth, survival, and fertility of mice, rats, and rabbits (*Oryctolagus cuniculus*) (Talamantes and Jang 1977; International Agency for Research on Cancer 1979; Klaassen et al. 1986; USEPA 1988; Khasawinah and Grutsch 1989; Ambrose et al. 1953; Cassidy et al. 1994).

6.4.2 TRVs

Table D-21 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-21 Mammal Chlordane TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	2.1	21	Narotsky and Kavlock 1995 (rat reproduction and growth)	1	a, b

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Source:
1 = TRV derived for the NBSA BERA

The LPRSA BERA (Windward 2019) and the LPR FFS (USEPA 2014) did not develop TRVs for chlordane; therefore, the TRVs used were developed specific to the NBSA site. The NBSA TRV came from a study by Narotsky and Kavlock (1995), where pregnant rats were fed chlordane by gavage over the period of gestation (6 to 19 days). The LOAEL represents the threshold of developmental effects, specifically, there was a reduction in postnatal survival and a weight gain in pups. A NOAEL was not available from the study and was estimated from the LOAEL using an extrapolation factor of 10. While there are uncertainties with these TRVs because they are based on a single study and there are no comparative TRVs from other risk evaluations in the region--the LPRSA BERA (Windward 2019) and the LPR FFS (USEPA 2014). Positive aspects of the Narotsky and Kavlock (1995) study are that the endpoints of reproduction and growth are likely more sensitive than mortality and required a sufficient exposure time to observe these endpoints.

7 ORGANOCHLORINE PESTICIDES – HEXACHLOROBENZENE

Hexachlorobenzene (HCB) is a chlorinated organic compound that was historically used extensively as a seed dressing to prevent fungal disease on grains, as a fungicide for a variety of crops, and in manufacturing processes. The use and manufacture of HCB ceased in the 1970s in the United States, and other countries due to concerns about its toxicological properties, persistence in the environment, and potential to bioaccumulate (Euro Chlor 2002). HCB continues to be released to the environment from a number of sources, including the use of some chlorinated pesticides; incomplete combustion; old dump sites; and inappropriate manufacture and disposal of wastes from the manufacture of chlorinated solvents, chlorinated aromatics, and chlorinated pesticides (ATSDR 2015).

HCB adsorbs readily to sediment or suspended particulate matter and bioaccumulates in food webs. Organisms generally accumulate HCB from water and from food, although benthic organisms may also accumulate HCB directly from sediment (Oliver 1984; Knezovich and Harrison 1988; Gobas et al. 1989). Significant bioaccumulation of HCB in fish, marine mammals, birds, and other animals has been observed. HCB does not degrade in water or sediment either by abiotic means or through biodegradation processes and undergoes limited metabolism due to its high chemical stability, making it very persistent in the environment (ATSDR 2015).

HCB has a variety of toxicological effects on the liver, ovary, skin, bone, and thyroid and causes, neurological, developmental, endocrine, and immunological toxicity in a variety of animals (ATSDR 2015; WHO 1995). Repeated exposure to HCB has also been shown to affect a wide range of organ systems (including the liver, lungs, kidneys, thyroid, skin, and nervous and immune systems (ATSDR 2015). More specific ecotoxicity information is provided below by receptor group.

7.1 Benthic Invertebrates

7.1.1 Toxicity Profile

Plankton, shellfish, and other invertebrates accumulate HCB from water and particles, and therefore, are important sources of HCB in aquatic food webs (Barber et al. 2005). Available data indicate that concentrations near the solubility limit of HCB (6 µg/L) should not cause acute toxicity (USEPA 1988).

Adverse effects of HCB in invertebrates have been reported for crayfish, water fleas, amphipods, and snails (*Lymnaea palustris*). Reported adverse effects include reduced egg production and increased mortality (Baturo et al. 1995; Baturo and Lagadic 1996), damage to the hepatopancreas (Laseter et al., 1976), reduced fertility (Calamari et al., 1983), and significantly increased mortality (Nebeker et al. 1989). In laboratory sediment toxicity studies, no effects on survival, growth or reproduction of the amphipod *Hyallela azteca* or the worm *Lumbriculus variegatus* were reported after exposure to HCB (Nebeker et al. 1989).

7.1.2 TRVs

Table D-22 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-22 Benthic Invertebrate Hexachlorobenzene TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	10.6	15.8	Nebeker et al. 1989 (amphipod mortality)	1,2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = TRV derived for the NBSA BERA
2 = LPRSA BERA (Windward 2019) Appendix A3-1

Hexachlorobenzene was not a COPEC evaluated in either the LPRSA BERA (Windward 2019) or the LPR FFS (USEPA 2014); however, TRVs were available in the LPRSA BERA Appendix A3-1. The selected TRVs came from the study by Nebeker et al. (1989) who examined hexachlorobenzene chronic toxicity to a water flea (*Daphnia*), two types of amphipods (*Hyalella*, *Gammarus*), a worm (*Lumbriculus*), and a minnow (*Pimphales*). These tests showed that hexachlorobenzene was largely non-toxic showing an absence of toxicity to the five test species based on no observed effects on growth or reproduction. The LOAELconcentration of 15.8 mg/kg ww was selected as a TRV and in the freshwater amphipod (*Gammarus lacustris*), which showed a 40% mortality after water exposure to hexachlorobenzene for 28 days. The NOAEL concentration from the same study (10.6 mg/kg ww) resulted in 20% mortality and was selected as a TRV (Nebeker et al. 1989).

7.2 Fish

7.2.1 Toxicity Profile

Fish accumulate chemical substances either directly from the surrounding environment or from their diet, with the largest proportion of HCB intake occurring from the diet. Bioaccumulation is affected by factors such as concentrations in prey, food web complexity, and the traits of individual fish such as growth rate and lipid content (ATSDR 2015). There is a strong relationship observed between HCB concentration and lipid content. Thus, fatty fish species accumulate more than lean fish species. HCB accumulates in fish tissues with high lipid content (Niemi 1986) such as liver tissue (Barber et al. 2005).

No adverse effects of HCB on survival, hematocrit, or plasma cortisol levels were found in Gulf killifish (*Fundulus grandis*) (Laska et al. 1978). Adverse effects on the liver were reported for largemouth bass (Laseter et al. 1976). Carlson and Kosian (1987), Schuytema et al. (1990), and Nebeker et al. (1989) found increased mortality and reduced growth in fathead minnows after exposure to HCB.

7.2.2 TRVs

Table D-23 summarizes the fish TRVs used in the assessment, and the section below describes how they were derived.

Table D-23 Fish Hexachlorobenzene TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	468	Not derived	Schuytema et al. 1990 (fathead minnow mortality)	1,2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = TRV derived for the NBSA BERA
2 = LPRSA BERA (Windward 2019) Appendix A3-1

Hexachlorobenzene was not a COPEC evaluated in either the LPRSA BERA (Wndward 2019) or the LPR FFS (USEPA 2014); however, TRVs were available in the LPRSA BERA Appendix A3-1. The NBSA NOAEL TRV of 468 mg/kg bw/day is based on a study of fathead minnow mortality after a 28-day exposure to aqueous hexachlorobenzene by Schuytema et al. (1990). A LOAEL was not derived from the study, and a LOAEL TRV was not estimated from the NOAEL. There are several uncertainties with the use of this NOAEL TRV: 1) the study failed to find an effect level, so is likely over-protective; and 2) the mortality endpoint is typically not as sensitive as sublethal endpoints.

7.3 Birds

7.3.1 Toxicity Profile

Adverse effects of HCB have been observed in Japanese quails, herring gulls (*Larus argentatus*), ring-necked pheasants, mallard ducks, and Eurasian kestrels (*Falco tinnunculus*). Reported adverse effects include induction of porphyria (Buhler and Carpenter 1986; Lambrecht et al. 1988); reduced embryonic body weight (Boersma et al. 1986); reduced body weight in adults (Schwetz et al. 1974); tremors, liver toxicity and increased mortality (Hill et al. 1975); and decreased egg production (Vos 1971; Vos et al. 1972).

7.3.2 TRVs

Table D-24 summarizes the bird TRVs used in the assessment, and the section below describes how they were derived.

Table D-24 Bird Hexachlorobenzene TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	1.1	5	Vos et al. 1971 (Japanese quail mortality)	1,2	a
Bird egg	mg/kg	70	265	Avrahami and Steele 2012 and Vos et al 1971 (Japanese quail mortality)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = TRV derived for the NBSA BERA
2 = LPRSA BERA (Windward 2019) Appendix A3-1

Hexachlorobenzene was not a COPEC evaluated in either the LPRSA BERA (Windward 2019) or the LPR FFS (USEPA 2014); however, TRVs were available in the LPRSA BERA Appendix A3-1. Both the LOAEL and the NOAEL come from a study by Vos et al. (1971). In this study Japanese quail were exposed to hexachlorobenzene in the diet for 90 days and mortality was observed. The NOAEL TRV came from the same study. The primary uncertainty with these TRVs is the general lack of toxicity information on the adverse effects to birds exposed to hexachlorobenzene in their diet.

Bird egg residues for hexachlorobenzene from which TRVs could be developed were not found during a literature search. However, there was an opportunity to develop a regression between food dose and egg concentrations of hexachlorobenzene (linear regression $r^2 = 0.998$). The regression equation applied to the food concentrations of 20 mg/kg and 80 mg/kg, which were the basis of the dietary NOAEL and LOAEL TRVs respectively, resulted in estimated egg concentrations of 70 mg/kg (NOAEL) and 265 mg/kg (LOAEL).

7.4 Mammals

7.4.1 Toxicity Profile

Adverse effects of HCB reported for mammals include liver toxicity, histopathological changes, liver enzyme induction, weight loss, neurological effects, porphyria, reduced litter sizes, and decreased survival and growth in offspring in rats and mink (Grant et al. 1977; Bleavins et al. 1984; WHO 1995; Courtney 1979; USEPA 1985; Strik 1986; Lilienthal et al. 1996; Arnold et al. 1985).

7.4.2 TRVs

Table D-25 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-25 Mammal Hexachlorobenzene TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	0.013	0.13	Bleavins et al. 1984 (mink reproduction)	1,2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = TRV derived for the NBSA BERA
2 = LPRSA BERA (Windward 2019) Appendix A3-1

Hexachlorobenzene was not a COPEC evaluated in either the LPRSA BERA (Windward 2019) or the LPR FFS (USEPA 2014); however, TRVs were available in the LPRSA BERA Appendix A3-1. The LOAEL concentration represents a significant reduction in birth weight in ferrets following 332 days of dietary exposure to hexachlorobenzene (Bleavins et al. 1984). A NOAEL was not available from this study and was extrapolated from the LOAEL using a factor of 10. There are several uncertainties with the use of a single study LOAEL TRV; although, the length of the study and the reproduction endpoint suggest that it is likely protective of the health of other species. In general, there is a lack of information on the adverse effects to mammals exposed to hexachlorobenzene including the fact that there are no comparative TRVs from other risk evaluations in the region – the LPRSA BERA (Windward 2019) and the LPR FFS (USEPA 2014).

8 POLYCYCLIC AROMATIC HYDROCARBONS

Polycyclic aromatic hydrocarbons (PAHs) are a large group of organic chemicals composed of two or more fused benzene rings (USEPA 2003b; ATSDR 1995). PAHs in the environment originate primarily from two sources: petrogenic (i.e., petroleum sources, including different types of oils, coal, and organic shales) and pyrogenic (i.e., combustion), with the majority associated with pyrogenic sources. Petrogenic PAHs are usually associated with local or point sources such as refineries and other petroleum industries, while pyrogenic PAHs tend to occur on a broader scale.

There are more than 100 individual PAHs, which are generally grouped into two categories: low-molecular-weight PAHs (LPAHs) (compounds composed of fewer than four benzene rings) and high-molecular-weight PAHs (HPAHs) (compounds composed of four or more benzene rings). Total PAHs is the sum of 16 individual PAHs that are commonly present in environmental mixtures and are known or suspected to contribute to toxicity. Total PAHs include seven LPAHs (acenaphthene, acenaphthylene, anthracene, fluoranthene, fluorene, naphthalene, and phenanthrene) and nine HPAHs (benzo(a)anthracene, benzo(a)pyrene, benzo(b/j)fluoranthene, benzo(g,h,i)perylene, benzo(k)fluoranthene, chrysene, dibenz(a,h)anthracene, indeno(1,2,3-cd)pyrene, and pyrene). In general, LPAHs have a greater tendency to volatilize and a lesser tendency to bind to organic carbon than do HPAHs, resulting in a lower persistence in the aquatic environment. Correspondingly, HPAHs are more likely to bioaccumulate than LPAHs and are more persistent in the environment. Bioaccumulation by upper-trophic-level organisms, including fish, birds, and mammals, is limited, in part because PAHs are known to be metabolized by fish (Khairy et al. 2014; Eisler 2000).

Photo-oxidation and chemical oxidation are important degradation processes for PAHs in water (Eisler 2000; ATSDR 1995). PAHs can also be chemically oxidized by chlorination and ozonation. Photolysis, hydrolysis, and chemical oxidation are generally not considered important degradation processes for PAHs in soils and sediments, especially for HMW PAHs (ATSDR 1995). Data suggest that naphthalene and phenanthrene may biodegrade most readily in water; anthracene, benzo(a)anthracene, chrysene, and fluorene may biodegrade in sediment water/slurries; and benzo(a)pyrene, dibenzo(a,h)anthracene, benzo(g,h,i)perylene, and other PAHs with five or more rings may not biodegrade readily at all (ATSDR 1995).

PAHs are lipophilic and can rapidly bioaccumulate from water, sediments, soil, and food. Less soluble PAHs are typically taken up more readily in the gastrointestinal tracts of animals (Eisler 2000). In general, bioconcentration is higher for HMW than LMW PAHs, but can vary by taxa based on the ability of organisms to metabolize parent PAHs to other compounds (ATSDR 1995). Fish can metabolize PAHs in the liver and excrete the metabolites in feces and urine. Most crustaceans also possess the required enzymes for metabolism. Organisms tend to take up PAHs easily from food, although dietary exposure sometimes contributes a limited amount to body burdens compared to water exposure. Due to metabolic ability, PAH concentrations in fish are typically low. Some data suggest that skin, as well as lipids, may be a temporary site of accumulation and may pose a barrier to the migration of PAHs in tissues. Mollusks and some other invertebrates may be unable to metabolize PAHs efficiently, although they can eliminate them. Studies of marine mollusks have found that while LMW PAHs were bioconcentrated more or less than HMW PAHs, the LMW PAHs were more readily eliminated. Sediment can also be a significant source of body burdens of PAHs for benthic invertebrates and fish. Biomagnification through aquatic food

webs has not been observed, likely due to rapid biotransformation and elimination (USEPA 2003b; Eisler 2000; ATSDR 1995).

The toxicity, carcinogenicity, and mutagenicity of PAHs vary with the molecular weight of the compound, the degree of alkylation, and the mode of accumulation (water, food, or sediment) by the organism (Eisler 2000; Moore and Ramamoorthy 1984; Neff 1979). LPAHs generally have significant acute toxicity, whereas HPAHs do not. However, several HPAHs are known to be carcinogenic and cause chronic toxicity. Thus, effects are highly dependent on the specific PAHs present in the environmental mixture and also upon the feeding behavior and habitat of a particular species. More specific ecotoxicity information is provided below by receptor group.

8.1 Benthic Invertebrates

8.1.1 Toxicity Profile

PAHs can be directly toxic to benthic invertebrates living in sediments, and also accumulated by these organisms because they lack the enzyme systems to metabolize and excrete them. Eisler (2000) reports PAH accumulations in marine organisms and notes that more water soluble, lower molecular weight PAHs are more easily accumulated than high molecular, weightless water-soluble PAHs, and there can be seasonal differences in PAH accumulations related to seasonal changes in lipids (Eisler 2000). For example, PAHs in oysters (Ostreidae) were higher in cooler months, when lipids and glycogen were being stored. Spawning results in a release of lipid-rich tissues and, therefore, a depuration of PAHs. Adverse effects observed in mussels (Mytilidae), like cellular proliferative disorders, look very similar to neoplastic conditions observed in invertebrates (Eisler 2000). Eisler (2000) also noted that age and body size can affect the degree of PAH accumulation, as demonstrated in the lobster (Nephropidae), where larger and older individuals had accumulated more PAHs.

8.1.2 TRVs

Table D-26 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-26 Benthic Invertebrate Total PAH TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Total LPAH						
Benthic invertebrate whole-body tissue	mg/kg ww	11	111	Lee et al. 2002 (amphipod mortality)	1	a,b
		0.078	0.780	Emery and Dillon 1996 (polychaete worm reproduction)	2	a
Total HPAH						
Benthic invertebrate whole-body tissue	mg/kg ww	8.1	22.2	Shuler et al 2007 (amphipod growth and reproduction)	1	a
		0.066	0.66	Blue mussel; reproduction (Eertman et al. 1995)	2	a,b

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

The LPRSA BERA found two studies evaluating LPAH toxicity to invertebrates, one for fluorene and one for naphthalene. The lowest LOAEL of 111 mg/kg ww (Lee et al. 2002) showed increased mortality in *Hyalella azteca* following 10 days of exposure to aqueous fluorene and was selected as the LOAEL TRV. No NOAEL was identified from this study; therefore, it was extrapolated from the LOAEL using a factor of 10. There is uncertaintly associated with the use of an extrapolation factor with the selected TRVs for fluorene due to the limited dataset (only two toxicity studies measuring mortality), and in comparing TRVs based on a single PAH (fluorene) to a concentration based on an LPAH sum.

The LPR FFS (USEPA 2014) selected an LPAH LOAEL TRV of 0.78 mg/kg ww and a NOAEL TRV of 0.078 mg/kg ww for LPAH based on an 8-week chronic toxicity study of the polychaete (*Nereis arenaceodentata*) exposed to phenanthrene (Emery and Dillon 1996). The LOAEL TRV of 0.78 mg/kg ww was associated with a 33% decrease in fecundity and a 36% decrease in juvenile production relative to the carrier control (acetone) group but was not different from the seawater control. Based on variable response in the two controls tested, there is uncertainty associated with whether an adverse effect would be expected. The NOAEL was extrapolated from the LOAEL using a factor of 10.

Eleven studies on seven species were found that examined growth, reproduction, and mortality resulting from exposure to single HPAHs (fluoranthene, benzo(a)pyrene and pyrene); no HPAH mixture studies were found. The lowest LOAEL, 22.2 mg/kg ww, was associated with a reduced length and reduced number of offspring of the amphipod *H. azteca* following a 28-day exposure to aqueous fluoranthene (Schuler et al. 2007). No adverse effects were observed in this study at a tissue burden of 8.1 mg/kg ww;

this value was selected as the NOAEL TRV. There is also uncertainty associated with comparing TRVs based on a single PAH (fluoranthene) to a concentration based on sum total HPAHs.

The LPR FFS derived a LOAEL TRV of 0.660 mg/kg ww and a NOAEL TRV of 0.066 mg/kg ww from this LOAEL using an extrapolation facor of 10 (USEPA 2014) based on a study that observed adverse effects on gametogenesis in blue mussels after a five-week exposure period to fluoranthene in water at a concentration of 2 µg/L (Eertman et al. 1993; Eertman et al. 1995). Eertman et al. (1993) presented data for tissue concentrations after a four-week exposure period to fluoranthene concentrations of 0.5, 1, and 6 µg/L. The LOAEL TRV of 0.66 mg/kg ww was estimated from regression relationships developed for tissue concentrations, water concentrations, and length of exposure. It is unclear what effect the impaired gametogenesis would have on population-level reproductive success. There is also uncertainty associated with estimating the LOAEL tissue concentration from data for different water concentrations and a shorter time period, comparing TRVs based on a single PAH (fluoranthene) to a concentration based on an HPAH sum, and using an extrapolation factor to derive the NOAEL.

8.2 Fish

8.2.1 Toxicity Profile

A wide variety of biological effects have been reported in numerous fish species under laboratory conditions. Exposure to stable, nonpolar organic compounds, such as PAHs, is known to cause narcosis (a generalized toxic effect) and can be involved in mortality (Schultz 1989). Fish embryos exposed to aqueous PAH mixtures have been shown to exhibit syndromes of cardiac dysfunction, edema, spinal curvature, and reduction in the size of the jaw and other craniofacial structures (Incardona et al. 2004). Exposure to PAHs has also been linked to the development of tumors in fish. Biotransformation by the mixed-function oxidases (MFO) system in the fish liver can result in the formation of carcinogenic and mutagenic intermediates (Eisler 2000). Fish exposed to PAH-contaminated sediments through direct contact have been shown to exhibit increased incidence of skin and liver lesions and other deformities (Myers et al. 1994; Pinkney et al. 2000). In addition, reduced lifespan in fish has been linked to cancerous lesions (Johnson et al. 2002; Baumann et al. 1987; Pinkney et al. 2000; Myers et al. 1994).

Observed adverse effects on fish from dietary exposure to PAHs include decreased disease resistance of Chinook salmon (Palm et al. 2003); reduced growth of Chinook salmon, English sole (*Parophrys vetulus*), rainbow trout, and rockfish (Kim et al. 2008; Rice et al. 2000; Hendricks et al. 1985; Hart and Heddle 1991; Meador et al. 2006); and reduced survival of rainbow trout and grouper (Epinephelinae) (Hendricks et al. 1985; Wu et al. 2003). Recently, behavioral effects have also been observed in fish as a result of exposure to PAHs (and dioxins and PCBs) (Weis et al. 2011).

8.2.2 TRVs

Table D-27 summarizes the fish TRVs used in the assessment, and the section below describes how they were derived.

Table D-27 Fish Total PAH TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish diet	mg/kg bw/day	6.2	18	Meador et al. 2006 (Chinook salmon growth)	1,	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Source:
1 = LPRSA BERA (Windward 2019)

The selected TRVs were developed in the LPRSA BERA (Windward 2019), which found two acceptable studies examining the effects of dietary PAHs on growth and the immune system (associated with increased mortality) in one species (Chinook salmon). The LOAEL available from Meador et al. (2006), 18 mg/kg bw/day, was selected as the LOAEL TRV and is associated with a 9% reduction in the dry weight of fish after 53 days of exposure to a dietary PAH mixture. A NOAEL of 6.2 mg/kg bw/day was identified and selected from the same study to be the NOAEL TRV (Meador et al. 2006). The PAH mixture tested by Meador et al. (2006) was designed to resemble a field PAH mixture from the Duwamish River in Seattle, Washington, which may not be similar to the PAH chemical mixture in the NBSA. The LPR FFS (USEPA 2014) did not develop fish dietrary PAH TRVs.

8.3 Birds

8.3.1 Toxicity Profile

The most likely route of exposure to PAHs for birds is through diet (Malcolm and Shore 2003). Birds tend to metabolize and excrete much of their ingested PAH load (Näf et al. 1992). Metabolism of PAHs also occurs in ovo (Näf et al. 1992). Adverse effects of PAHs on birds observed in laboratory studies include reduced survival of bobwhite quails (Brausch et al. 2010) and mallard ducks (Patton and Dieter 1980), reduced fertility of pigeons (Columbidae) (Hough et al. 1993), reduced growth of chickens (Rigdon and Neal 1963) and mallard ducks (Patton and Dieter 1980), and reduced embryonic growth and an increase in the percent of embryonic anomalies in mallard (Hoffman and Gay 1981).

8.3.2 TRVs

Table D-28 summarizes the bird TRVs used in the assessment, and the section below describes how they were derived.

Table D-28 Bird Total PAH TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Total LPAH						
Bird diet	mg/kg bw/day	0.67	6.7	Schafer et al. 1983 (red-winged blackbird survival)	1	a, b
Total HPAH						
Bird diet	mg/kg bw/day	0.048	0.48	Hough el al. 1993 (pigeon reproduction)	1	a
Total PAH						
Bird diet	mg/kg bw/day	40	Not derived	Patton and Dieter 1980 (mallard duck growth)	2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Sources:
1 = LPR FFS (USEPA 2014)
2 = LPRSA BERA (Windward 2019)

The selected LOAEL and NOAEL TRVs for total LPAH were derived in the LPR FFS (USEPA 2014) and based on a study by Schafer et al. (1983), which demonstrated that various 2- and 3-ring PAHs (including acenaphthene, fluorene, anthracene, and phenanthrene) were acutely toxic (48-hr Lethal Dose to 50% [LD50]) in red-winged blackbirds at concentrations of approximately 100 mg/kg body weight. An extrapolation factor of five was used to estimate chronic effect levels, and an extrapolation factor of three was applied for interspecies variation to obtain the LOAEL TRV of 6.7 mg/kg ww. The NOAEL TRV of 0.67 mg/kg ww was estimated from the LOAEL TRV using an extrapolation factor of 10. The LPRSA BERA (Windward 2019) did not develop LPAH bird dietary TRVs.

The selected LOAEL and NOAEL TRVs for total HPAH were derived in the LPR FFS (USEPA 2014) and based on a study by Hough et al. (1993) that administered the benzo(a)pyrene dose to pigeons by weekly injection. There were no acceptable studies found that exposed birds to HPAH mixtures in the diet, which is why a single HPAH (benzo(a)pyrene) was selected and used as a surrogate for HPAHs. A LOAEL value of 1.4 mg/kg bw/day was based on observed cessation of egg laying in pigeons exposed for five months to this daily dose (Hough et al. 1993) and then dividing the weekly dose (10 mg/kg bw/day) by seven days to determine the daily dose exposure. This daily dose exposure was then divided by an interspecies extrapolation factor of three under the assumption that pigeons were three times less sensitive than the most sensitive avian species (USEPA 2014). The NOAEL (0.048 mg/kg/day was derived from the LOAEL (0.48 mg/kg/day) based on a factor of 10.The total PAH TRV came from the LPRSA BERA (Windward 2019). The TRV based on Patton and Dieter 1980 was selected by LPRSA BERA and was the only available acceptable study in LPRSA BERA Appendix A3-1 Table 6 that exposed birds to a PAH mixture in the diet. The NOAEL concentration represents no significant decrease in body

weight or survival of mallards fed a mixture of PAHs for seven months (Patton and Dieter 1980). The study did not report a LOAEL concentration. This mixture did not include the HPAH benzo(a)pyrene, which is a specific PAH constituent of concern in the NBSA BERA; therefore, this is an inherent uncertainty in this study.

8.4 Mammals

8.4.1 Toxicity Profile

Various studies have demonstrated the acute toxicity and reproductive toxicity of PAHs to laboratory mammals (WHO 1998), although research on PAH effects on wild mammals is uncommon and is generally associated with oil spills (e.g., Chapter 13 of Douben 2003). In MacKenzie and Angevine (1981), the exposure of mice to benzo(a)pyrene resulted in adverse effects on reproduction (decreased pup body weight and decreased adult male testes weights). Exposure to PAHs, including 1-methylnaphthalene, 2-methylnaphthalene, naphthalene, and benzo(a)pyrene, caused decreases in growth, survival and reproduction in laboratory studies of mice and rats (Murata et al. 1993; Hodson 1985; Neal and Rigdon 1967; Navarro et al. 1991; Leighton 1989; Rigdon and Neal 1965).

8.4.2 TRVs

Table D-29 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-29 Mammal Total PAH TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Total LPAH						
Mammal diet	mg/kg bw/day	50	150	Navarro et al. 1991 (rat growth)	1	a
Total HPAH and Total PAH						
Mammal diet	mg/kg bw/day	0.62	3.1	Culp et al. 1998 as cited in USEPA 2007d (mouse survival)	1,2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = LPR FFS (USEPA 2014)
2 = LPRSA BERA (Windward 2019)

The LPRSA BERA did not develop PAH TRVs (Windward 2019); both the LPAH and HPAH TRVs selected were developed in the LPR FFS (USEPA 2014), and were derived from USEPA's guidance on Eco SSL for PAHs (USEPA 2007b)., For LPAHs, the selected study was Navarro et al. (1991) in which 8-

to-10 week-old female Norway rats (*Rattus norvegicus*) were exposed to naphthalene in food for 9 days. Significant body weight effects were observed at the higher concentrations resulting in LOAEL and NOAEL TRVs are 150 and 50 mg/kg bw/day, respectively. For HPAHs, the selected study was Culp et al. (1998) in which juvenile mice were exposed to benzo(a) pyrene in food for 100 weeks. Significant and dose dependent mortality occurred at the higher concentrations resulting in LOAEL and NOAEL TRVs are 3.1 and 0.62 mg/kg bw/day, respectively. The fact that they are studies that passed the rigorous Eco SSL standards for selection and represent the lowest bounded results from the accepted studies reviewed provides credibility regarding their support. This NBSA BERA used the LPRSA BERA HPAH TRV as a surrogate for total PAH TRVs.

9 ARSENIC

Arsenic is a relatively common element that occurs in air, water, soil, and all living tissues (Eisler 2000). Arsenic is naturally present in rock and soils. Higher concentrations are associated with igneous and sedimentary rocks, particularly with sulfidic ores (USEPA 2005a; American Petroleum Institute 1998). Most arsenic produced domestically is used in manufacturing of agricultural products (e.g., insecticides, herbicides, fungicides, algicides, wood preservatives, and growth stimulants for plants and animals). Exposure to arsenic can occur by way of atmospheric emissions from smelters, coal-fired power plants, and arsenical herbicide sprays; from water contaminated by mine tailings, smelter wastes, and natural mineralization; and from diet, especially from consumption of marine biota (Eisler 2000).

Transport and partitioning of arsenic in water depends on the chemical form (oxidation state and counter ion) and interactions with other materials. Arsenic may be adsorbed from water onto sediments or soils, especially in clays, iron oxides, aluminum hydroxides, manganese compounds, and organic material. Soluble forms move with the water and may be carried long distances through rivers (ATSDR 2007a; USEPA 1979). Arsenic in the water column may be resuspended sediment. Arsenic bioaccumulates in animals and depends on the environmental setting, organism type, trophic status, exposure concentration, and route of uptake. It does not appear to biomagnify between tropic levels (ATSDR 2007a). Arsenic may be elevated in marine biota due to the ability of arsenic to accumulate from seawater or food sources (Maher 1985). The majority of arsenic in marine organisms exists as water-soluble and lipid-soluble organic arsenicals that include arsenolipids, arsenosugars, arsenocholine, arsenobetaine, monomethylarsonate, and demethylarsinate, as well as other forms (Eisler 2000). Toxic and other effects of arsenicals to aquatic life are significantly modified by numerous biological and abiotic factors, including water temperature, pH, redox conditions, organic matter, phosphate concentration, suspended solids, the presence of other substances and toxicants, arsenic speciation, and duration of exposure (Eisler 2000). In general, inorganic arsenicals are more toxic than organic arsenicals to aquatic biota, and trivalent arsenic species are more toxic than pentavalent arsenic species. Early life stages are most sensitive to arsenic, and differences in the ecotoxicological effects of arsenic among species are large, even among those closely related taxonomically (Eisler 2000). More specific ecotoxicity information is provided below by receptor group.

9.1 Benthic Invertebrates

9.1.1 Toxicity Profile

Bioconcentration of arsenic occurs in aquatic organisms, primarily in algae and lower invertebrates (ATSDR 2007a). Tissue concentrations of arsenic in marine biota are typically highest in lipids, then liver, and muscle tissues, and vary with organism age (Eisler 2000). Marine biota is able to accumulate arsenic from seawater or food sources, not due to localized pollution. The reason for this ability is not clear but may be related to an anabolic/catabolic pathway concerned with the synthesis and turnover of phosphatidylcholine (Eisler 2000). Most of the arsenic in marine organisms exists as a water-soluble and lipid-soluble organic arsenical form called arsenobetaine, which has little potential risks associated with consumption (Eisler 2000). Exposure to arsenic in invertebrate species including amphipods (*Hyalella azteca*), bay scallop (*Argopecten irradians*), brown shrimp, periwinkle snail (*Littorina littorea*), amphipod (*Corophium volutator*), Baltic clam (*Macoma balthica*), copepod (*Eurytemora affinis*), and oligochaete worm (*Tubifex costatum*) increased mortality (Bryant et al. 1985; Norwood et al. 2007; Klumpp 1980; Madsen 1992; Nelson et al. 1976), reduced juvenile survival (Sanders 1986), and reduced growth (Irving et al. 2008).

9.1.2 TRVs

Table D-30 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-30 Benthic Invertebrate Arsenic TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	0.064	0.64	SSD (Windward 2019)	1	a,b

Notes:
KU = Key Uncertainty
a = TRV based on an SSD
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Source:
1 = TRV derived for the LPRSA BERA (Windward 2019)

The LPRSA BERA (Windward 2019) developed an SSD from the seven studies found where LOAEL values ranged from 0.63 to 92 mg/kg ww. The 5th percentile of the SSD, 0.64 mg/kg ww, was selected as the LOAEL TRV, just above the lowerst measured LOAEL of 0.63 mg/kg ww. The NOAEL TRV of 0.064 mg/kg ww was extrapolated from the LOAEL TRV using an uncertainty factor of 10. There is uncertainty associated with the derivation of a NOAEL based on an extrapolation factor. No TRVs for arsenic were available in the LPR FFS (USEPA 2014).

9.2 Fish

9.2.1 Toxicity Profile

Although some fish and shellfish take in arsenic, which may build up in tissues, most of this arsenic is in an organic form called arsenobetaine (commonly called "fish arsenic") that is much less harmful (ATSDR 2007a). Arsenic is mainly accumulated in the livers of fish. Fish may bioaccumulate metals from water or from feeding on other fish, including bottom-feeders. The major bioaccumulation transfer is between water and algae, at the base of the food web, which has a strong impact on the concentration in fish. Differences in arsenic levels were not found in different species of fish, including herbivorous, insectivorous, and carnivorous species. Williams et al. (2006) found that accumulation in fish is nonlinear with respect to the exposure concentration (ATSDR 2007a).

Adverse effects of exposure to arsenic have been reported in rainbow trout, spottail shiner (*Notropis hudsonius*), fathead minnow, bluegill, pink salmon (*Oncorhynchus gorbuscha*), and grey mullet (*Chelon labrosus*). These include increased mortality (National Academy of Sciences [NAS] 1977; Lima et al. 1984; Taylor et al. 1985), reduced growth rates (Johnson and Finley 1980; NAS 1977), food avoidance (Johnson and Finley 1980; NAS 1977), and reduced food metabolism (Johnson and Finley 1980; NAS 1977).

9.2.2 TRVs

Table D-31 summarizes the fish TRVs used in the assessment, and the sections below describe how they were derived.

Table D-31 Fish Arsenic TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	1.3	2.5	Erickson et al. 2011 (rainbow trout growth)	1	a
Fish diet	mg/kg bw/day	0.52	1.9	Blazer et al. 1997 (striped bass growth)	2, 3	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)
2 = TRV derived for the NBSA BERA
3 = LPRSA BERA (Windward 2019) Appendix A3-1

9.2.2.1 Fish Whole-Body Tissue

Three studies examining growth, behavior, and mortality for one fish species (rainbow trout) provided three LOAELs that ranged from 2.5 to 8.1 mg/kg ww. The lowest LOAEL, from Erickson et al. (2011), was

selected as the NBSA LOAEL TRV as was used for the LPRSA BERA (Windward 2019). Erickson et al. (2011) exposed juvenile rainbow trout to aqueous arsenic for 28 days and reported a ≥ 25% reduction in growth at the LOAEL of 2.5 mg/kg ww (assuming 80% moisture). The NOAEL of 1.3 mg/kg ww (assuming 80% moisture) from the same study was selected as the NOAEL TRV. Erickson et al. (2011) also reported that surviving fish ranged up to 3.0 mg/kg ww arsenic in whole-body fish (assuming 80% moisture), and that mortality did not correlate well with total arsenic accumulation. Fish mortality appears to be less sensitive than growth and with a response that is not well correlated with arsenic tissue concentrations where critical concentrations ranged up to 12 mg/kg ww (Erickson et al. 2011; McGeachy and Dixon 1992). This suggests that risks are likely overestimated from the selected TRVs. The LPR FFS (USEPA 2014) did not develop fish whole-body TRVs for arsenic.

9.2.2.2 Fish Diet

Arsenic was not a fish dietary COPEC evaluated in either the LPRSA BERA (Windward 2019) or the LPR FFS (USEPA 2014); however, TRVs were available in the LPRSA BERA Appendix A3-1. Both of the dietary TRVs were based on the study by Blazer et al. (1997), where juvenile striped bass were fed arsenic-contaminated diets for 6 weeks. Adverse growth effects observed at the LOAEL concentration of 1.9 mg/kg bw/day are believed to be associated with food avoidance, which leads to some uncertainty in these TRVs because it is hard to relate dietary exposure concentrations to adverse effects when the fish are reducing their consumption level of food.

9.3 Birds

9.3.1 Toxicity Profile

Inorganic trivalent arsenite poisoning in birds may include muscular incoordination, debility, slowness, jerkiness, falling hyperactivity, fluffed feathers, drooped eyelid, huddled position, unkempt appearance, loss of righting reflex, immobility, and seizures, similar to many other toxicants (Eisler 2000). Nystrom (1984) suggests that lethal effects of acute inorganic arsenic poisoning were caused by destruction of blood vessels lining the gut, which resulted in decreased blood pressure and subsequent shock. Adverse effects of exposure to arsenic in mallard ducks, chukars (*Alectoris chukar*), California quails, bobwhite quails, and chickens include increased mortality (NAS 1977; NRCC 1978; Camardese et al. 1990), reduced growth (Camardese et al. 1990; Stanley et al. 1994), negative effects on reproductive success (NRCC 1978; Stanley et al. 1994), and embryonic developmental abnormalities (Hood 1985).

9.3.2 TRVs

Table D-32 summarizes the bird TRVs used in the assessment, and the section below describes how they were derived.

Table D-32 Bird Arsenic TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	10	40	Stanley et al. 1994 (mallard duck reproduction)	1,2	a

Notes:
KU = Key Uncertainty

a = TRV based on a single study

Source:
1 = TRV derived for the NBSA BERA
2 = LPRSA BERA (Windward 2019) Appendix A3-1

Arsenic was not a bird dietary COPEC evaluated in either the LPRSA BERA (Windward 2019) or the LPR FFS (USEPA 2014); however, TRVs were available in the LPRSA BERA Appendix A3-1 (Windward 2019). The LOAEL and NOAEL TRVs of 40 and 10 mg/kg bw/day, respectively, were based on a study of the effects of arsenic on mallard reproduction from a dietary exposure of 115 to 128 days (Stanley et al. 1994). Effects noted were delayed egg laying, depressed egg weight and shell thinning, decreased offspring body weight, and decreased production that were suspected to be the result of insufficient food intake (Stanley et al. 1994). These arsenic TRVs were selected for bird diet in the LPRSA SLERA (Windward 2019; Appendix A).

9.4 Mammals

9.4.1 Toxicity Profile

Mammals are primarily exposed to arsenic by ingestion of naturally contaminated vegetation and water or human activity. Acute arsenic poisoning in most warm-blooded animals is usually revealed by acute or subacute signs. Acute poisoning in mammals by inorganic and organic arsenicals are usually characterized by high mortality and morbidity over a period of 2 to 3 days and may include signs of intense abdominal pain, staggering gait, extreme weakness, trembling, salivation, vomiting, diarrhea, fast and feeble pulse, prostration, collapse, and death (Eisler 2000). Chronic poisoning is not often seen but is associated with weakness, paralysis, conjunctivitis, dermatitis, decreased growth, and liver damage (NRCC 1978).

9.4.2 TRVs

Table D-33 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-33 Mammal Arsenic TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	2.6	5.4	Byron et al. 1967 (rat growth)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Source:
1 = LPRSA BERA (Windward 2019)

The selected TRVs were developed in the LPRSA BERA (Windward 2019), which found only one acceptable study as the basis of the TRVs, Byron et al. (1967). The LOAEL of 5.4 mg/kg bw/day and the NOAEL of 2.6 mg/kg bw/day were based on rat growth and decreased body weight following dietary exposure to arsenic in the form of sodium arsenite(Bryon et al. 1967). There were no mammalian TRVs for arsenic developed for the LPR FFS (USEPA 2014).

10 CADMIUM

Most cadmium used in the United States is extracted as a byproduct during the production of other metals, such as zinc, lead, or copper. Most cadmium (83%) is used for batteries, with other minor uses for pigments (8%) and coatings and platings (7%) (ATSDR 2012a). Cadmium in the environment exists in only one oxidation state (+2) and does not undergo oxidation-reduction reactions. Specifically, cadmium in surface water can exist as soluble or insoluble forms: the hydrated ion, or as ionic complexes with other inorganic or organic substances. In polluted or organic-rich waters, adsorption of cadmium by humic substances and other organic complexing agents plays a dominant role in transport, partitioning, and remobilization of cadmium (ATSDR 2012a). Those forms likely to precipitate and not be remobilized include associations with carbonate minerals, or hydrous iron oxides. Cadmium more likely to be remobilized or bioaccumulated exists adsorbed to mineral surfaces, such as clay or organic materials.

Cadmium bioaccumulates in aquatic food webs, has no biological function, and is considered toxic to aquatic organisms (Eisler 2000). Sublethal effects of cadmium in marine animals include decreased growth, inhibited reproduction, respiratory disruption, altered enzyme levels, and abnormal muscular contractions; effects were usually most obvious at relatively low salinities and high temperatures (Eisler 2000). Sublethal effects of cadmium in birds, which were similar to those in other animals, included growth retardation, anemia, and testicular damage; however, these effects were observed at higher concentrations than in aquatic biota (Eisler 2000). More specific ecotoxicity information is provided below by receptor group.

10.1 Benthic Invertebrates

10.1.1 Toxicity Profile

Bioaccumulation data for invertebrates are reported substantially more than studies on toxicity. Adverse effects of exposure to cadmium in water fleas, mysid shrimp (*Mysidopsis* sp.), fiddler crab (*Uca pugilator*), Baltic clam, and the copepod (*Acartia tonsa*) include increased mortality (Duquesne et al. 2004), reduced growth (Smolders et al. 2005), decreased reproductive output (Canton and Slooff 1982; Bertram and Hart 1979; Hook and Fisher 2002), reduced biomass (Marshall 1978), molt inhibition (Gentile et al. 1982), and reduced respiration (Vernberg et al. 1974).

10.1.2 TRVs

Table D-34 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-34 Benthic Invertebrate Cadmium TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	0.024	0.24	SSD (Windward 2019)	1	a,b

Notes:
KU = Key Uncertainty
a = NOAEL estimated from a LOAEL with an extrapolation factor of 10
b = TRV based on an SSD

Source:
1 = LPRSA BERA (Windward 2019)

The LPRSA BERA (Windward 2019) developed an SSD from the 60 studies found where LOAEL values ranged from 0.02 to 3,400 mg/kg ww. The 5th percentile of the SSD, 0.24 mg/kg ww, was selected as the LOAEL TRV, within the range of measured LOAEL values. The NOAEL TRV of 0.024 mg/kg ww was extrapolated from the LOAEL TRV using an uncertainty factor of 10. There is uncertainty associated with the derivation of a NOAEL based on an extrapolation factor. No TRVs for cadmium were available in the LPR FFS (USEPA 2014).

10.2 Fish

10.2.1 Toxicity Profile

In fish, acute cadmium toxicity is dependent in part on exposure period, concentration, water temperature and salinity, although the mechanisms of toxicity are not well understood (Eisler 2000). Under conditions of high cadmium concentration and short exposure, the gill seems to be the primary site of damage and accumulation. Under conditions of prolonged exposure and low cadmium levels, the intestine, kidney, and possibly other tissues were measurably affected. Retention of cadmium by fish depends on tissue biomagnification potential, length of post-exposure recovery period, and other factors (Eisler 2000).

Adverse effects of exposure to cadmium in brook trout, channel catfish, and walleye (*Stizostedion vitreum*) include reductions in growth, survival, and fecundity (Brungs et al. 1978; Eisler 2000). Adverse effects of exposure to cadmium in striped bass, winter flounder, Atlantic salmon, mummichog, and Asian seabass (*Lates calcarifer*) include increased mortality (Eisler 1971; Shazili 1995), reduced growth (Kim et al. 2004; Kang et al. 2005; Lundebye et al. 1999), enzyme disruption and decreased oxygen consumption (Dawson et al. 1977), and increased gill tissue respiration (Calabrese et al. 1975).

10.2.2 TRVs

Table D-35 summarizes the fish TRVs used in the assessment, and the section below describes how they were derived.

Table D-35 Fish Cadmium TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish diet	mg/kg bw/day	0.001	0.01	Kim et al. 2004, Kang et al. 2005 (rockfish growth)	1	a, b

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Source:
1 = LPRSA BERA (Windward 2019)

The NBSA LOAEL and NOAEL TRVs of 0.001 and 0.01 mg/kg bw/day, respectively, were based on a study of the effects of cadmium on rockfish growth from a dietary exposure of 60 days (Kim et al. 2004; Kang et al. 2005) that were developed in the LPRSA BERA (Windward 2019). This LOAEL was the lowest of four other LOAELs from three other studies reviewed in the LPRSA BERA (Windward 2019). The LOAEL represents a dietary concentration of 125 mg/kg dry weight (dw), and the NOAEL represents a dietary concentration of 25 mg/kg dw. The NOAEL was estimated from the LOAEL using an extrapolation factor of 10. There is uncertainty associated with the use of an extrapolation factor to derive the NOAEL. No TRVs for cadmium in the fish diet were available from the LPR FFS (USEPA 2014). Cadmium was not a COPEC for fish tissue.

10.3 Birds

10.3.1 Toxicity Profile

In general, birds are more resistant to adverse effects from cadmium than lower trophic level aquatic organisms (USEPA 1999b). Sparrows fed a diet with radio-labeled cadmium showed that the cadmium goes to the kidney and liver (Eisler 2000). Sublethal effects of cadmium in birds, which were similar to those in other animals, included growth retardation, anemia, and testicular damage. Cadmium has a greater likelihood of causing teratogenic effects than other metals (lead, mercury, copper, indium, and arsenic) (Eisler 2000). In birds, this has been reported as caudal and hindlimb abnormalities observed in chickens that resulted from injection of eggs with 0.1 to 1.0 ppm of cadmium chloride. These adverse effects were reduced in the presence of zinc (Ferm and Layton 1981).

Sublethal effects of exposure to cadmium in birds, including Japanese quails, ringed turtle-doves, chickens, domestic pigeons, and mallard ducklings, include growth retardation and anemia (Hammons et al. 1978); bone marrow hypoplasia, anemia, and heart hypertrophy (Richardson et al. 1974); anemia, an enlarged heart, myocardial infarction, and other cardiovascular abnormalities (Sturkie 1973); testicular damage (Sarkar and Mondal 1973); and altered blood chemistry and kidney lesions (Cain et al. 1983). Altered avoidance behavior in the form of hyperresponsiveness was observed in young American black ducks (*Anas rubripes*) produced from parents fed 4 ppm dietary cadmium for about 4 months before egg laying (Heinz and Haseltine 1983).

10.3.2 TRVs

Table D-36 summarizes the bird TRVs used in the assessment, and the section below describes how they were derived.

Table D-36 Bird Cadmium TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	0.4	4	Richardson et al. 1974 (Japanese quail growth)	1	a, b

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Source:
1 = LPRSA BERA (Windward 2019)

The selected TRVs were derived in the LPRSA BERA (Windward 2019), which found six studies with three species were acceptable for the derivation of a cadmium TRVs for birds. The lowest LOAEL of 4.0 mg/kg bw/day was selected as the TRV based on a 6-week exposure to cadmium in the diet of Japanese quail (Richardson et al. 1974). This LOAEL represents a 15% reduction in body weights as comparted to the controls. A NOAEL was not available from this study, so it was estimated from the LOAEL TRV using an uncertainty factor of 10. An uncertainty specific to this study is whether a 15% reduction in growth would result in adverse effects on the population; thus, the TRVs are likely overestimates of potential adverse effects. No TRVs for cadmium in the bird diet were available from the LPR FFS (USEPA 2014).

10.4 Mammals

10.4.1 Toxicity Profile

In vertebrates, cadmium accumulates in the liver and kidneys (ATSDR 2012a), and mammals are less sensitive to adverse effects from cadmium than aquatic organisms (USEPA 1999b). There is strong evidence for food web bioaccumulation, but the potential for biomagnification is uncertain. Eisler (2000) reported the potential for teratogenic effects with the examples of rat fetuses with jaw defects, cleft palates, club feet, and pulmonary hyperplasia following exposure to more than 6 mg/kg ww daily during pregnancy and hamsters with embryonic tail defects following cadmium exposure. It was also noted that in the study with hamsters, effects were synergized by salts of lead or mercury and antagonized by selenium (Ferm and Layton 1981).

10.4.2 TRVs

Table D-37 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-37 Mammal Cadmium TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	3.5	13	Machemer and Lorke 1981 (rat growth)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Source:
1 = LPRSA BERA (Windward 2019)

The selected TRVs were developed for the LPRSA BERA (Windward 2019), which evaluated three acceptable studies of cadmium toxicity on mammals (rats and shrews). The selected LOAEL, 13 mg/kg bw/day, was the lowest of the studies evaluated and represented decreased maternal body weight of rats exposed to dietary cadmium chloride (Machemer and Lorke 1981). The NOAEL of 3.5 mg/kg bw/day also came from Machemer and Lorke (1981). No TRVs for cadmium in the mammal diet were available from the LPR FFS (USEPA 2014).

11 CHROMIUM

Mining and the combustion of fossil fuels and other materials may cause releases of chromium to air, surface water, and soil. These anthropogenic activities lead to the production of hexavalent chromium, which is very mobile and relatively stable in air and pure water and, therefore, may be subject to long-distance transport. However, upon contact with organic matter or biota, hexavalent chromium is reduced to its trivalent form (WHO 1988). That form clings to particles, which may be deposited onto soil or sediment. Once in soil, chromium tends to be immobile due to the formation of stable organic complexes. Even low pH is not able to leach chromium from soil. Trivalent chromium in water may form polynucleate complexes that are no longer soluble and precipitate out of the water column. As a result, soluble chromium generally accounts for a very small percentage of total chromium. Chromium compounds cannot volatilize from water, so most of the chromium released into water will ultimately be deposited in the sediment. Plants and animals may absorb both the hexavalent and trivalent forms of chromium (WHO 1988); however, the hexavalent form is taken up in preference to the trivalent form. Once absorbed, hexavalent chromium is reduced to the stable, trivalent state. Bioaccumulation from all exposure routes and toxicity of trivalent chromium is low relative to hexavalent chromium, because the latter is more membrane permeable and corrosive (USEPA 1999b). Trivalent chromium in vertebrates is an essential nutrient required for normal energy metabolism (ATSDR 2012b).

There is no indication of biomagnification of chromium in food webs, and chromium concentrations typically are highest at the lowest trophic levels (WHO 1988; Eisler 2000). Reported toxic effects of chromium in aquatic organisms include reduced survival, reproduction, and growth. Under laboratory conditions, chromium has been shown to be mutagenic, carcinogenic, and teratogenic in a wide variety of organisms, with hexavalent chromium being the primary toxic form. These effects are modified by a variety of biological and abiotic factors and sensitivity to chromium varies widely, even among closely related species (Eisler 2000). More specific ecotoxicity information is provided below by receptor group.

11.1 Benthic Invertebrates

11.1.1 Toxicity Profile

Chromium in surface waters may remain in a soluble form or it may bind to clay-like or organic-suspended solids. Exposure routes for aquatic organisms include ingestion, gill uptake, and dermal absorption (USEPA 1999b), and bioaccumulation in benthic invertebrates occurs. Measurable accumulations were recorded in oysters and worms (Annelida) at 5.0 µg/L of hexavalent chromium, and reproduction of polychaete annelid worms (Polychaeta) was inhibited at 12.5 µg/L. Hexavalent chromium was associated with adverse effects in invertebrates of widely separated taxa: growth inhibition of the protozoan *Chilomonas paramecium* (Honig et al. 1980); abnormal movement patterns of larvae of the midge *Chironomus tentans* (Catalan 1982); and a temporary decrease in hemolymph glucose levels in the freshwater prawn *Macrobrachium lamarrei* (Murti et al. 1983). A reduction in offspring numbers in the polychaete *Neanthes arenaceodentata* occurred after exposure to chromium (Oshida and Word 1982). In all situations, trivalent chromium was found to be less toxic than hexavalent chromium.

11.1.2 TRVs

Table D-38 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-38 Benthic Invertebrate Chromium TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	1.5	3.5	Norwood et al. 2007 (amphipod survival and growth)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study
Source:
1 = LPRSA BERA (Windward 2019)

Two studies were found that reported chromium toxicity to benthic invertebrates and the lowest LOAEL from these studies, 3.5 mg/kg ww, from Norwood et al. (2007) was selected as the LOAEL TRV. This study exposed *H. azteca* to water- and diet-based chromium for four weeks and recorded mortality. The NOAEL of 1.5 mg/kg ww was equivalent to the LC25 and was within the range of control mortality in the same study. There is uncertainty associated with the limited toxicity dataset for chromium (two studies). No TRVs for chromium were available in the LPR FFS (USEPA. 2014).

11.2 Fish

11.2.1 Toxicity Profile

Chromium uptake and effects in fish are modified by many biological and abiotic variables, including water temperature and pH, the presence of other contaminants or compounds, and sex and tissue specificity (Eisler 2000). Reduced growth was observed after dietary exposure to chromium in the tilapia (Magzoub et al. 2010) and grey mullet (Walsh et al. 1994). In the snakehead (*Channa punctatus*), enzyme activities were altered in a wide variety of organs and tissues after exposure to chromium (Sastry and Sunita 1984) and caused increased mortality (Sastry and Sunita 1982, 1983). In the mud skipper (*Boleophthalmus dussumieri*), chromosomal aberrations in the gill increased after exposure to chromium (Krishnaja and Rege 1982). In juvenile coho salmon, disease resistance and serum agglutinin production both decreased after exposure to chromium (Sugatt 1980). In Chinook salmon, exposure to chromium increased mortality (Farag et al. 2006).

11.2.2 TRVs

Table D-39 summarizes the fish TRVs used in the assessment, and the sections below describe how they were derived.

Table D-39 Fish Chromium TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	1.28	1.3	Farag et al. 2006 (Chinook salmon mortality)	1	a
Fish diet	mg/kg bw/day	0.19	Not derived	Walsh et al. 1994 (grey mullet growth)	2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = TRV derived for the NBSA BERA
2 = LPRSA BERA (Windward 2019)

11.2.2.1 Fish Whole-Body Tissue

NBSA TRVs were both derived from Farag et al. (2006), who exposed Chinook salmon to chromium for 134 days. The LOAEL TRV of 1.3 mg/kg ww represents a 27% reduction in survival. The NOAEL of 1.28 mg/kg ww from the same study was associated with a 12% reduction in survival, which was not significantly different from the control.

No TRVs for chromium were available from either the LPRSA BERA (Windward 2019) or the LPR FFS (USEPA 2014); although, Farag et al. (2006) was one of three studies evaluated in the LPRSA BERA and had the lowest reported LOAEL and the LOAEL and NOAEL concentrations as reported in Table D-39. The LPRSA BERA excluded Farag et al. (2006) as the basis of a TRV because of the increase in the exposure concentration on day 105 of the 134 day exposure period. These TRVs were accepted for the NBSA BERA because the increase in exposure was warranted because on day 105 no adverse effects were observed in the fish. The subsequent 29 day exposure at a higher concentration did elicit adverse effects.

11.2.2.2 Fish Diet

The TRVs selected were derived in the LPRSA BERA (Windward 2019), which found two studies available for the derivation of chromium dietary TRVs for fish. Neither study identified a LOAELs, so the study with the highest NOAEL (0.92 mg/kg bw/day) was selected as the NOAEL TRV (Walsh et al. 1994). This study exposed grey mullet to chromium in both sediment and diet. At 0.19 mg/kg bw/day, the chromium-exposed fish showed a significant increase in growth, which is not considered an adverse effect. There is uncertainty associated with the use of an unbounded NOAEL, as it may over-predict the potential for a NOAEL. The LPR FFS (USEPA 2014) did not develop fish dietary TRVs for chromium.

11.3 Birds

11.3.1 Toxicity Profile

Most investigators agree that chromium in biological materials is probably always in the trivalent state (Eisler 2000). Acute and chronic adverse effects to warm-blooded organisms are caused mainly by hexavalent chromium compounds. There is little conclusive evidence of toxic effects caused by di- or trivalent chromium (Langard and Norseth 1979).

For birds, chromium exposure through diet adversely affected young American black ducks (Eisler 2000). Deformities in birds include short and twisted limbs, microphthalmia, exencephaly, everted viscera, growth stunting, and parrot beaks (Ridgeway and Karnofsky 1952; Gilani and Marano 1979). Male domestic chickens, fed diets containing up to 100 ppm of hexavalent chromium for 32 days, showed no adverse effects in survival, growth, or food utilization efficiency (Rosomer et al. 1961), but teratogenic effects were documented in chicken embryos after eggs had been injected with hexavalent chromium. The highest incidence of teratogenic effects was observed at hexavalent chromium concentrations that caused some deaths. American black ducklings that were fed chromium-contaminated diets exhibited altered growth patterns and reduced survival (Eisler 2000). When the administration route was through the chorioallantoic membrane (as opposed to the yolk), no teratogenic effects were observed with trivalent chromium salts (Ridgeway and Karnofsky 1952).

11.3.2 TRVs

Table D-40 summarizes the bird TRVs used in the assessment, and the section below describes how they were derived.

Table D-40 Bird Chromium TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	10.5	105	Chung et al. 1985 (chicken survival and growth)	1	a, b

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Source:
1 = LPRSA BERA (Windward 2019)

The TRVs selected were derived in the LPRSA BERA (Windward 2019), which found four studies, all with chickens, acceptable for derivation of chromium dietary TRVs for birds. None of these studies found adverse effects on bird reproduction. The lowest LOAEL from these studies, 105 mg/kg bw/day, was selected as the TRV and was based on adverse effects on growth and survival (Chung et al. 1985). There was no NOAEL available from this study, so the NOAEL TRV was estimated from the LOAEL using an extrapolation factor of 10. One additional study conducted with mallards (Haseltine et al. unpublished) was cited in Sample et al. (1996), but the data are unpublished and unavailable for review. The

unpublished study (Haseltine et al. unpublished) reportedly found reproductive effects on American black duck (*Anas rubripes*) at a dietary dose of 5 mg/kg bw/day. This effect level was the lowest LOAEL among the five chromium studies. However, because the original data could not be reviewed, this value was not selected as the LOAEL TRV for the NBSA BERA.

11.4 Mammals

11.4.1 Toxicity Profile

As stated above for birds, acute and chronic adverse effects to warm-blooded organisms are caused mainly by hexavalent chromium compounds (Eisler 2000). In mammals, hexavalent chromium compounds may cause skin ulceration, irritative dermatitis, ulcerations in mucous membranes, and perforations of the nasal septum (Eisler 2000). Dietary levels of 5.1 mg/kg hexavalent chromium in the food and water of mice was associated with elevated tissue residues. Kidney and liver lesions in rats were observed when the drinking water contained 134 ppm of hexavalent chromium for 2 to 3 months (Steven et al. 1976). Chromium is causally associated with mutations and malignancy (Leonard and Lauwerys 1980; Norseth 1981). Exposure to dietary chromium in rats caused decreased body weight and growth (Hasten et al. 1997; Ivankovic and Preussman 1975), increased mortality (Anderson et al. 1997; Ivankovic and Preussman 1975), and reduced litter size and pregnancy rate and increased pup malformation (Ivankovic and Preussman 1975). Under appropriate conditions, chromium is an animal carcinogen; however, its toxicological effects depend on chemical form, solubility, and valence. In general, hexavalent chromium compounds are hazardous to animals, whereas metallic chromium and trivalent chromium are essentially nontoxic (Gale 1978); however, exposure to water-solubilized trivalent chromium has caused cancers and dermatitis in workers and toxicity in rabbits (Hatherill 1981).

11.4.2 TRVs

Table D-41 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-41 Mammal Chromium TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	0.96	9.62	Zahid et al. 1990, as cited in USEPA 2008b (mouse reproduction)	1	a,b

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Source:
1 = TRV derived for the NBSA BERA

The chromium LOAEL TRV of 9.62 mg/kg bw/day was derived from the USEPA (2008b) Chromium Eco SSL report and, specifically, the study by Zahid et al. (1990), which reported reproductive effects in mice. A NOAEL was not available from this study and was extrapolated from the LOAEL using a factor of 10. No chromium dietary TRVs for mammals were available from the LPRSA BERA (Windward 2019) or the LPR FFS (USEPA 2014).

12 COPPER

Copper is a naturally occurring and ubiquitous metal found throughout the Earth's crust. While low levels of copper are important for good health (copper is an essential element for plants and animals, including humans), high levels of copper can be harmful to health or the environment. Copper is extensively mined in the United States to produce various products, including electrical wires, plumbing components, and alloys used in other products. Additionally, copper compounds are used in agricultural settings (e.g., for treating plant diseases, such as mildew); for water treatment; and as a preservative in products, such as wood and fabrics (ATSDR 2004).

Copper can enter the environment through human activities, including mining, smelting, and releases of wastewater, and through natural sources, such as volcanoes or forest fires. Copper found in the environment is usually associated with organic material or other soil/sediment components, such as clay or sand. Once released into the environment, copper does not break down, meaning that once it enters the water, it builds up in the sediments of lakes and rivers. It can be found in high concentrations in animal species (ATSDR 2004).

Copper, at elevated levels of exposure, can exert a wide range of physiological effects in animals, including altered blood chemistry, and is associated with tissue structure and pathology of kidneys, liver, gills, and other hematopoietic tissues (Eisler 2000). More specific ecotoxicity information is provided below by receptor group.

12.1 Benthic Invertebrates

12.1.1 Toxicity Profile

In aquatic organisms, exposures to copper are associated with developmental abnormalities. Copper bioconcentrates in aquatic organisms; however, biomagnification does not occur. For many animals, copper is an essential micronutrient (USEPA 1999b). Most of the copper in aquatic environments settles out and adsorbs to sediment, but this is dependent on water pH and temperature and the concentration of other chemical species (USEPA 1999b). In aquatic invertebrates, copper causes gill damage at high concentrations (Eisler 2000).

Copper-stressed blue mussels die more quickly under conditions of anoxia, high temperatures, and low salinities (Weber et al. 1992). Initial effects of copper on mussels (*Mytilus* spp.) include valve closure, a reduction in filtration rates, and cardiac inhibition; these responses all serve to slow the uptake of copper through a reduction in mussel contact with the ambient environment and a reduction in blood flow within the organism (Gainey and Kenyon 1990).

Life-cycle exposures of four daphnid species to copper show reductions in survival, growth, and reproduction (Winner and Farrell 1976). In shore crabs (*Carcinus maenas*), several days of exposure to sublethal concentrations of waterborne copper caused extensive damage to gill epithelium; at lethal concentrations, tissue hypoxia was the major effect of copper (Nonnotte et al. 1993). Increases in mortality have been observed after exposure to copper for shrimp (*Mysis* spp.) (Zyadah and Abdel-Baky

2000), polychaete worm (*Cirriformia spirabrancha*) (Milanovich et al. 1976), and clams (*Mysella anomalia*) (King et al. 2004).

12.1.2 TRVs

Table D-42 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-42 Benthic Invertebrate Copper TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	5	12	Absil et al. 1996 (Baltic clam survival)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Source:
1 = LPR FFS (USEPA 2014)

The NBSA TRVs of 12 mg/kg ww for the LOAEL and 5 mg/kg ww for the NOAEL were obtained from the ERED and, specifically, the study by Absil et al. (1996) in which the sediment-dwelling bivalve (*Macoma balthica*) exposed to copper for 40 days showed mortality at tissue concentrations of 12 mg/kg ww, but no significant mortality at tissue concentrations of 5 mg/kg ww. These same TRVs were used in the LPR FFS (USEPA 2014).

12.2 Fish

12.2.1 Toxicity Profile

Copper can cause toxicity in fish by interfering with osmoregulation (Eisler 2000). Adverse effects, including reduced growth and survival, were reported in toxicological studies of five fish species (Atlantic salmon, channel catfish, rainbow trout, rockfish, and grey mullet) following dietary exposure to copper. A reduction in growth was reported in a study of rockfish and grey mullet, decreased weight was reported in a study of channel catfish fingerlings, and decreased survival was reported in a study of rainbow trout (Berntssen et al. 1999a, 1999b; Baker et al. 1998; Handy 1992, 1993; Kamunde et al. 2001; Kang et al. 2005; Lanno et al. 1985a, 1985b; Lundebye et al. 1999; Miller et al. 1993; Mount et al. 1994; Murai et al. 1981).

12.2.2 TRVs

Table D-43 summarizes the fish TRVs used in the assessment, and the sections below describe how they were derived.

Table D-43 Fish Copper TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	3.92	4.48	Mount et al. 1994 (rainbow trout mortality)	1,3	a
		0.32	1.5	Zyadeh and Abdel-Baky 2000 (striped mullet [*Mugil cephalus*] survival)	2	a
Fish diet	mg/kg bw/day	1	2	Kang et al. 2005 (rockfish growth)	3	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = TRV derived for the NBSA BERA
2 = LPR FFS (USEPA 2014)
3 = LPRSA BERA (Windward 2019)

12.2.2.1 \Fish Whole-Body Tissue

NBSA TRVs were derived from Mount et al. (1994), who exposed rainbow trout to copper in the diet for 60 days and found reduced survival associated with a whole-body concentration of 4.48 mg/kg ww, which was selected as the LOAEL. From the same study, a NOAEL tissue concentration of 3.92 mg/kg ww was selected.

The LPRSA BERA concluded no studies reporting tissue body burdens greater than the nutritionally optimal copper body burden of 3.4 mg/kg ww were acceptable for TRV development. Therefore, no TRVs for copper in whole-body fish were used in the LPRSA BERA (Windward 2019). Mount et al. (1994) was one of five studies evaluated in the LPRSA BERA, and had the second lowest reported LOAEL; the lowest LOAEL was for effects observed in Nile tilapia (*Oreochromis niloticus*), which was not considered to be a relevant fish species for the NBSA. The LPRSA identified the same endpoint concentrations as shown in Table D-43, but the study was excluded as the basis of TRVs because at the two points when tissue concentrations were measured, day 35 and day 60, tissue burdens were found to be higher on day 35 by approximately 45 to 55% as compared to the concentrations on day 60, yet no mortality was observed on day 35.

An acute study (24 hrs) by Zyadeh and Abdel-Baky (2000) that exposed striped mullet to aqueous copper was the basis of the TRVs used in the LPR FFS (USEPA 2014). The exposure concentration of 10 milligram per liter (mg/L) resulted in a tissue concentration of 7.5 mg/kg ww and was a mortality LOAEL. The tissue concentration was selected as the LOAEL TRV after application of an ACR extrapolation factor of 5, resulting in a LOAEL TRV of 1.5 mg/kg ww. The NOAEL TRV (0.32 mg/kg ww) was derived from the same study based on application of the same ACR to the tissue residue of 1.6 mg/kg ww, resulting from an exposure of 5 mg/L.

12.2.2.2 Fish Diet

The selected TRVs were derived in the LPRSA BERA (Windward 2019) and based on a review of 13 toxicity studies on the effects of dietary copper to four species of fish (Atlantic salmon, grey mullet, rainbow trout, and rockfish). These data were not sufficient to develop an SSD. The seven reported LOAELs ranged from 2.0 to 60 mg/kg bw/day. The lowest LOAEL of 2.0 mg/kg bw/day was selected as the TRV and was associated with a 50% reduction in rockfish growth after 60 days of exposure to copper in the form of a pelletized diet (Kang et al. 2005). The NOAEL of 1.0 mg/kg bw/day from this same study was selected as the NOAEL TRV. The LPR FFS (USEPA 2014) did not develop copper dietary TRVs.

Regarding the potential for uncertainties in these TRVs, Clearwater et al. (2002) indicated that daily doses of copper that caused adverse effects appeared to be fairly consistent within species for a given life stage with the sources of variability attributed to 1) the way the copper was administered in the diet, since copper chelates to organic compounds, thus altering bioavailability; and 2) water quality (especially temperature and possibly salinity).

12.3 Birds

12.3.1 Toxicity Profile

A review of laboratory studies using birds found that adverse effects on growth and survival were observed as a result of dietary exposure to copper. In studies of young chicks exposed to copper, reduced growth was observed during subchronic exposures (25 days), and reduced growth and survival were observed during chronic exposure (10 weeks) (Mehring et al. 1960; Persia et al. 2004; Dozier et al. 2003; Smith 1969; Balevi and Coskun 2004; Lien et al. 2004; Poupoulis and Jensen 1976).

12.3.2 TRVs

Table D-44 summarizes the bird TRVs used in the assessment, and the section below describes how they were derived.

Table D-44 Bird Copper TRVs

Tissue	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	1.9	19	Jensen and Maurice 1978 (chicken growth)	1	a, b
		2.3	4.7	Kashani et al. 1986, as cited in USEPA 2007a (wild turkey [Meleagris gallopavo] growth)	2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10
Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

The selected TRVs were derived in the LPRSA BERA (Windward 2019) where eight studies, all with chickens, were acceptable for the derivation of TRVs for copper toxicity to birds. The lowest LOAEL,19 mg/kg bw/day, was selected as the TRV based on a 10% reduced growth of chicks as compared to the control following 4 weeks of dietary exposure (Jensen and Maurice 1978). A NOAEL was not available from the study, so the NOAEL TRV was estimated from the LOAEL using an extrapolation factor of 10. An uncertainty with this study is that adverse population effects are not anticipated from a 10% reduction in the growth of chicks. Thus, the TRVs are likely to overestimate the potential for adverse effects.

The LPR FFS (USEPA 2014) developed a LOAEL TRV of 4.7 mg/kg ww and a NOAEL TRV of 2.3 mg/kg ww for copper based on USEPA's Eco SSL report for copper USEPA (2007a). The LOAEL TRV was based on a 4% decrease in body weight in wild turkeys compared to the control after 8 weeks of exposure, noting, however, that body weight recovered at 12 weeks and that no further effects on body weight were observed at 16, 20, or 24 weeks (Kashani et al. 1986). An uncertainty with this study is that adverse population effects are not anticipated from a 4% reduction in growth of chicks, particularly since these growth effects recovered by 12 weeks and were not again observed throughout the 24-week study. Thus, the TRVs are likely to overestimate the potential for adverse effects.

12.4 Mammals

12.4.1 Toxicity Profile

The exposure of mammals to copper has been reported to adversely affect reproduction, growth, and survival. Effects of exposure to copper include decreased growth for mice, reduced reproduction (reduced kit survival) for mink, and reduced growth for rats (National Institutes of Health 1993; Aulerich et al. 1982; Dodds-Smith et al. 1992). Of the three species examined in these studies (mink, rats, and mice), mink was determined to be the species that was most sensitive to copper exposure.

12.4.2 TRVs

Table D-45 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-45 Mammal Copper TRVs

Tissue	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	18	26	Aulerich et al. 1982, as cited in USEPA 2007a (mink reproduction)	1	a
		3.4	6.8		2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study
Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

The selected TRVs were developed in the LPRSA BERA (Windward 2019) where four acceptable toxicity studies were available from the literature in which mammals (rats, mice, shrew, and mink) were exposed to dietary copper. The selected TRVs were based on the mink study by Aulerich et al. (1982) and the endpoints of decreased kit survival and litter mass where the LOAEL was 26 mg/kg bw/day and the NOAEL was 18 mg/kg bw/day.

The LPR FFS (USEPA 2014) selected LOAEL and NOAEL TRVs of 6.8 and 3.4 mg/kg bw/day, respectively, which were also based on Aulerich et al. (1982) andon USEPA's Eco SSL report for copper (USEPA 2007a). However, the endpoint was different: the number of kits whelped. Specific uncertainties related to this study were: 1) there were no observations at the LOAEL of statistically identifiable effects on kit mortality, kit growth, or the average number of kits whelped per female; and 2) the number of females whelping per exposure group was not dose responsive (12 out of 12 whelped in the mink fed 50 mg/kg in the diet).

13 LEAD

Lead is a naturally occurring metal found in the Earth's crust. Lead can be found throughout the environment, largely as a result of anthropogenic activities, such as mining, burning of fossil fuels, and various manufacturing processes. Lead is currently mined in the United States for use in products, such as pipes, batteries, and ammunition. The use of lead in other products (e.g., caulking materials and pigments for paints and ceramic glazes) has been greatly reduced due to health concerns associated with exposure to lead. Historically, lead has been used in pesticides in fruit orchards (starting in the early 1900s) and as an additive to gasoline (between 1950 and 2000) to increase engine efficiency; both of these uses occurred worldwide (ATSDR 2007b).

Once lead enters the environment, its particulates in the air are subject to atmospheric transport and deposition, allowing lead to enter sediment, soil, or surface water. Lead strongly sorbs to soil and sediment and generally will not leach into subsurface soil and groundwater. Lead in surface water exists primarily in an undissolved phase (i.e., as lead carbonate, lead oxide, and lead hydroxide) (ATSDR 2007b). In aquatic environments, benthic organisms and algae have the highest lead concentrations. Higher-trophic-level species may experience toxic effects as a result of increased lead concentrations in their diet (ATSDR 2007b; Eisler 2000).

Lead can adversely affect survival, growth, reproduction, development, and metabolism of many species under controlled conditions, but its effects are substantially modified by numerous physical, chemical, and biological variables. Adverse effects on aquatic biota include reduced survival, impaired reproduction, reduced growth, and high bioconcentration from the medium (Eisler 2000). Among sensitive species of birds and mammals, survival and reproduction were impaired, and signs of poisoning were evident at low lead ingestion doses (Eisler 2000). In general, routes of administration other than lead ingestion are unlikely to cause clinical signs of lead poisoning in birds and mammals. In general, organic lead compounds are more toxic than inorganic lead compounds, and food-web biomagnification of lead is negligible (Eisler 2000). More specific ecotoxicity information is provided below by receptor group.

13.1 Benthic Invertebrates

13.1.1 Toxicity Profile

Lead bioaccumulation in aquatic species is usually highest in algae and benthic organisms and lowest in upper-trophic-level predators, but lead has been shown to be toxic to all trophic levels (Eisler 2000). Lead exposure increased mortality for Indian prawn shrimp (*Penaeus indicus*) (Chinni et al. 2002), reduced reproductive output and caused immobilization in *Daphnia magna* (USEPA 1985; Berglind et al. 1985; Demayo et al. 1982), reduced hatching success in the snail (*Lymnaea palustris*) (Borgmann et al. 1978), inhibited development in the sea urchin (*Anthocidaris crassispina*) (Kobayashi 1971), and inhibited reproduction in the polychaete *Neanthes arenaceodentata* (USEPA 1985).

13.1.2 TRVs

Table D-46 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-46 Benthic Invertebrate Lead TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	4	40	Spehar et al. 1978 (amphipod survival)	1	a,b
		0.52	2.6	Borgmann and Norwood 1999 (amphipod survival)	2	a

Notes:
[1] = Total TEQ refers to total dioxin/furan TEQ, total PCB TEQ, and total PCB and dioxin/furan TEQ
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10
Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

Three studies were found that reported lead toxicity to benthic invertebrates and the lowest LOAEL from these studies, 40 mg/kg ww, from Spehar et al. (1978) was selected as the LOAEL TRV. This study exposed the amphipod *G. psuedolimnaeus* to water-based lead concentrations for 28 days and recorded mortality. A NOAEL was not available from this study and was estimated from the LOAEL using an extrapolation factor of 10. There is uncertainty in using an extrapolation factor to derive a NOAEL.

The LOAEL (2.6 mg/kg ww) and NOAEL (0.52 mg/kg ww) derived in the LPR FFS (USEPA 2014) were also used as TRVs. Both were from the study by Borgmann and Norwood (1999) and based on increased mortality of the amphipod *H. azteca* in a four-week spiked sediment toxicity test. The LOAEL was derived from the LC25 and the NOAEL TRV was derived using an extrapolation factor of five applied to the LOAEL. There is uncertainty associated with the derivation of a NOAEL based on an extrapolation factor.

13.2 Fish

13.2.1 Toxicity Profile

Lead exposure in fish has been shown to cause increased mucous formation, which coagulates over the entire body and is particularly prominent over the gills, interfering with respiratory function and resulting in death by anoxia (Aronson 1971; NRCC 1973). Fish, including, brook trout, rainbow trout, rosy barb (*Puntius conchonius*), zebrafish (*Brachydanio rerio*), and coho salmon that are continuously exposed to elevated concentrations of waterborne lead show various signs of lead poisoning, including: spinal curvature; anemia; darkening of the dorsal tail region, producing a black-tail effect due to selective destruction of chromatophores but not of melanophores; degeneration of the caudal fin; destruction of spinal neurons; reduced ability to swim against a current; destruction of the respiratory epithelium; basophilic stippling of erythrocytes; muscular atrophy; paralysis; renal pathology; growth inhibition; retardation of sexual maturity; altered blood chemistry; testicular and ovarian histopathology; and death (Aronson 1971; NRCC 1973; Adams 1975; Davies et al. 1976; Holcombe et al. 1976; Hodson et al. 1977,

1980, 1982; Johansson-Sjobeck and Larsson 1979; Reichert et al. 1979; Ozoh 1980; Demayo et al. 1982; Kumar and Pant 1984; Rai and Qayyum 1984; Hodson and Spry 1985; Haux et al. 1986).

13.2.2 TRVs

Table D-47 summarizes the fish TRVs used in the assessment, and the sections below describe how they were derived.

Table D-47 Fish Lead TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	2.5	4.0	Holcombe et al. 1976 (brook trout growth)	1	a
		0.4	4.0	Holcombe et al. 1976 (brook trout reproduction)	2	a, b
Fish diet	mg/kg bw/day	12.6	Not derived	Mount et al. 1994 (rainbow trout growth)	3	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)
3 = TRV derived for the NBSA BERA

13.2.2.1 Fish Whole-Body Tissue

LOAELs were available for two species of fish (fathead minnow and brook trout), ranging from 4.0 to 26.2 mg/kg ww. Holcombe et al. (1976) exposed juvenile brook trout to water-based lead concentrations for 3 generations over 3 years, resulting in the lowest reported LOAEL; this study was selected for TRV derivation. A LOAEL of 4.0 mg/kg ww (assuming 80% moisture) was identified and associated with decreased egg hatchability of the third generation of fish. No effects on survival, growth, or reproduction were observed at this exposure level in the preceding two generations; however, there was a clear dose-response relationship for increased scoliosis that affected spawning behavior. A NOAEL of 2.5 mg/kg ww (assuming 80% moisture) was also identified from the same study. These values were selected as TRVs. The paucity of data increased the uncertainty of the selected TRVs.

The LPR FFS (USEPA 2014) also selected a LOAEL TRV of 4.0 mg/kg ww based on data from Holcombe et al. (1976); however, the endpoint selected was different – reproductive (i.e., deformed spines in third-generation fish). The NOAEL of 0.4 mg/kg ww was extrapolated from the LOAEL using an uncertainty factor of 10. There is uncertainty associated with the use of an extrapolation factor to derive the NOAEL.

13.2.2.2 Fish Diet

The NBSA LOAEL TRV for lead was based on the study by Mount et al. (1994), who exposed rainbow trout to lead in the diet for 60 days and found no reduced survival associated with the highest test concentration of 12.6 mg/kg bw/day, which was selected as the NOAEL TRV. No LOAEL TRV was available from this study, and one was not estimated using extrapolation factors. The LPRSA BERA (Windward 2019) and LPR FFS (USEPA 2014) did not develop fish dietary TRVs for lead. There is uncertainty in estimating the potential for adverse effects from an unbounded NOAEL and that the TRV was based on a single study.

13.3 Birds

13.3.1 Toxicity Profile

Lead accumulated in aquatic vertebrates tends to increase with increasing age of the organism and tends to deposit in hard tissues, such as bone and teeth (Eisler 2000). Adverse effects on birds, as a result of dietary exposure to lead, have been studied for a variety of bird species, including domesticated birds (chicken and Japanese quail) and non-domesticated birds (American kestrel, mallard duck, and ringed turtle-dove) (Kendall and Scanlon 1982; Hoffman et al. 1985; Pattee 1984; Edens et al. 1976). These studies found decreased reproductive success in Japanese quail based on decreases in egg production and hatchability (Morgan et al. 1975; Edens et al. 1976). Numerous laboratory studies found other adverse effects, including damage to the nervous system, muscular paralysis, kidney and liver damage, internal lesions, enlarged gall bladder, anemia, reduced brain weight, and abnormal skeletal development – all of which cause a decrease in survival (Eisler 2000).

13.3.2 TRVs

Table D-48 summarizes the bird TRVs used in the assessment, and the section below describes how they were derived.

Table D-48 Bird Lead TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	5.5	28	Morgan et al. 1975 (Japanese quail growth)	1	a
		0.19	1.9	Edens and Garlich 1983, as cited in USEPA 2005d (Japanese quail reproduction)	2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

The selected TRVs were developed in the LPRSA BERA (Windward 2019) where seven studies were found acceptable for the derivation of dietary TRVs, and four of these were prioritized as the basis because they were dietary studies of lead toxicity to birds. The lowest of the four dietary LOAELs, 28 mg/kg bw/day, was selected as the TRV and was based on a 5-week exposure of Japanese quail that noted an adverse effect on growth (Morgan et al. 1975). Specifically, the effect noted was a 10% decrease in body weight compared to the control. The NOAEL from the same study, 5.5 mg/kg bw/day, was selected as the NOAEL TRV. An uncertainty with this study is that there are unknown potential population level impacts from a 10% reduction in growth.

The LPR FFS (USEPA 2014) selected LOAEL and NOAEL TRVs of 1.9 and 0.19 mg/kg bw/day, respectively, based on USEPA's Eco SSL report for lead USEPA (2005d). These TRVs were based on Japanese quail egg production using data from Edens and Garlich (1983). An uncertainty with this study is that Japanese quails, like chickens, are a domesticated species with reproductive rates that are bred to be higher than wildlife; therefore, the implications for wildlife reproduction rates are unknown.

13.4 Mammals

13.4.1 Toxicity Profile

The exposure of mammals to high concentrations of lead in the diet has been reported to cause anemia, weight loss, muscle atrophy, paralysis, brain damage, mortality, and reproductive effects (Eisler 2000). Toxicity studies on dietary exposure to lead in mammal species (mouse and rat) reported adverse effects on reproduction, growth, and behavior. These effects included decreased offspring survival, decreased litter size, decreased offspring weight, decreased adult body weight, and decreased liver and kidney weight (Odenbro and Kihlstrom 1977; Schroeder and Mitchener 1971; Overmann 1977; Azar et al. 1973; Wise 1981; Iavicoli et al. 2006).

13.4.2 TRVs

Table D-49 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-49 Mammal Lead TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	11	90	Azar et al. 1973 (rat; growth)	1	a
		0.71	7.0	Grant et al. 1980, as cited in USEPA 2005d (rat reproduction)	2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study
Source:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

The selected TRVs were developed in the LPRSA BERA (Windward 2019) where three acceptable toxicity studies were available from the literature in which mammals were exposed to dietary lead in the form of lead acetate. Two studies evaluated growth in rats (Azar et al. 1973) and mice (Wise 1981), and one study evaluated reproduction in mice (Iavicoli et al. 2006). Azar et al. (1973) reported the lowest LOAEL, 90 mg/kg bw/day, which resulted in decreased body weight of rat offspring. The NOAEL from this study was 11 mg/kg bw/day (Azar et al. 1973) and was also selected as a TRV. There is uncertainty associated with the limited number of dietary studies identified from the literature review.

The LPR FFS (USEPA 2014) selected a LOAEL TRV and NOAEL TRV of 7.1 and 0.71 mg/kg bw/day, respectively, which was based on USEPA's Eco SSL report for lead (USEPA 2005d). These TRVs were developed from a study of rats exposed to lead in drinking water and noted adverse effects on reproduction (Grant et al. 1980).

14 MERCURY/METHYLMERCURY

Mercury is a naturally occurring metal that is present in various forms, including elemental mercury, inorganic mercury (primarily as mercuric salts), and organic mercury (primarily methylmercury). Elemental and inorganic mercury can enter the environment as by-products of industrial and commercial operations (e.g., mining, emissions from coal-fired power plants, and incineration of waste-containing mercury) as well as through natural processes (e.g., weathering of rocks that contain mercury). In addition, before the 1970s (i.e., when the health effects of methylmercury were unknown), methylmercury was used as a fungicide to protect seed grain (ATSDR 1999).

Recycling of mercury in the environment often involves elemental mercury volatilizing from surface soils and waters, followed by atmospheric transport and deposition back to surface soils and waters. Mercury can also be associated with air particulates, but it is unlikely to be transported long distances (ATSDR 1999).

Mercury and its compounds have no known biological function, and the presence of mercury in the cells of living organisms is undesirable and potentially hazardous (Eisler 2000). Forms of mercury with relatively low toxicity can be transformed into forms of very high toxicity, such as methylmercury, by microorganisms in soil, sediment, and water. Methylmercury is important with regard to ecological risks, because it is soluble and mobile, rapidly bioaccumulates in aquatic organisms, and concentrates in the tissues of carnivorous fish and other organisms. It is also known to be more toxic and bioaccumulative than elemental and inorganic mercury (ATSDR 1999). Mercury is a known mutagen, teratogen, and carcinogen. At comparatively low concentrations in birds and mammals, mercury adversely affects reproduction, growth and development, behavior, blood and serum chemistry, motor coordination, vision, hearing, histology, and metabolism. Signs of acute mercury poisoning in fish include flaring of gill covers, increased frequency of respiratory movements, loss of equilibrium, and sluggishness (Eisler 2000). Signs of chronic mercury poisoning include emaciation (due to appetite loss), brain lesions, cataracts, diminished response to change in light intensity, inability to capture food, abnormal motor coordination, and various erratic behaviors (Eisler 2000). More specific ecotoxicity information is provided below by receptor group.

14.1 Benthic Invertebrates

14.1.1 Toxicity Profile

Mercury exposure adversely affects the reproduction, growth, behavior, metabolism, blood chemistry, osmoregulation, and oxygen exchange of marine and freshwater organisms. In general, the accumulation of mercury by aquatic biota is rapid, and depuration is slow. Organomercury compounds, especially methylmercury, were significantly more likely to induce adverse effects than inorganic mercury (Eisler 2000). Mercury exposure caused adverse effects on the reproduction (spawning delay, reduced fecundity, population declines) of sensitive species of aquatic organisms, including slipper limpet (*Crepidula fornicate*) and mysid shrimp (*Mysidopsis bahia*) (Gentile et al. 1983).

Reduced growth of sensitive species of aquatic organisms was found in the marine mollusc (*Crepidula fornicate*) (Thain 1984) and sea urchin larvae (USEPA 1980a). In marine molluscs exposed to mercury, the feeding of adults ceased, and the swimming rate of larval stages declined (Thain 1984).

14.1.2 TRVs

Table D-50 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-50 Benthic Invertebrate Mercury and Methylmercury TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	0.048	0.095	Hook and Fisher 2002 (copepod reproduction)	1, 2	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

The selected TRVs were derived from a study by Hook and Fisher (2002) and were also used in the LPRSA BERA (Windward 2019) and the LPR FFS (USEPA 2014). Three studies on three invertebrate species were available and reviewed for the development of a mercury TRV for invertebrates, including two zooplankton (copepod and cladoceran) studies and one bivalve study (eastern oyster). The copepod study (Hook and Fisher 2002) had the lowest LOAEL (0.095 mg/kg ww) and represented tissue residues associated with a 50% reduction in the number of eggs produced. This LOAEL was selected as the TRV. The selected NOAEL TRV (0.048 µg/kg ww) also came from the same study.

14.2 Fish

14.2.1 Toxicity Profile

Adverse effects on five fish species (i.e., fathead minnow, golden shiner [*Notemigonus crysoleucas]*, walleye, mummichog, and rainbow trout), resulting from exposure to methylmercury in toxicological studies, included effects on growth, survival, and reproduction. Specifically, reduced survival was observed in male mummichog and rainbow trout, and reduction of growth and abnormalities in gonadal development were observed in juvenile walleye (Friedmann et al. 1996; Hammerschmidt et al. 2002; Matta et al. 2001; Rodgers and Beamish 1982; Webber and Haines 2003; Sandheinrich and Miller 2006). The exposure of mummichog, golden shiner, mosquitofish (*Gambusia affinis*), and largemouth bass to methylmercury resulted in increased mortality due to observed behavioral effects (e.g., altered male behavior and altered predator avoidance) that increased predation (Webber and Haines 2003; Kania and O'Hara 1974; Matta et al. 2001).

14.2.2 TRVs

Table D-51 summarizes the fish TRVs used in the assessment, and the sections below describe how they were derived.

Table D-51 Fish Methylmercury TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	0.035	0.35	Windward 2019 (12 species SSD)	1	a, b
		0.052	0.26	Beckvar et al. 2005 (seven species; growth, survival, reproduction, and behavior)	2	a, b
Fish egg	mg/kg ww	0.006	0.06	Birge et al. 1979 (channel catfish reproduction)	1, 2	b, c
Fish diet	mg/kg bw/day	0.00056	0.0056	Windward 2019 (10 species SSD)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on an SSD
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10 or 5
c = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

14.2.2.1 Fish Whole-Body Tissue

The NOAEL and LOAEL TRVs of 0.035 and 0.35 mg/kg ww, respectively, for methylmercury derived in the LPRSA BERA (Windward 2019) were based on an SSD using 17 LOAELs for 12 species of fish reported in 14 studies based on the adverse effects on behavior, growth reproduction, or survival. Eight of these studies used dietary exposures and the other six used water exposures. LOAELs ranged from 0.47 to 22 mg/kg ww and the 5th percentile of the SSD (0.35 mg/kg ww) was less than the lowest acceptable LOAEL and was the selected LOAEL TRV for the LPRSA BERA (Windward 2019). The NOAEL TRV (0.035 mg/kg ww) was extrapolated from the LOAEL TRV using an uncertainty factor of 10. There is uncertainty associated with the derivation of a NOAEL based on an extrapolation factor.

The LPR FFS (USEPA 2014) TRVs were derived from an SSD developed by Beckvar et al. (2005) with seven species of fish, where the selected TRV LOAEL of 0.26 µm/kg ww represents the 5th percentile LOAEL using data derived from ERED. The selected TRV NOAEL of 0.052 mg/kg ww was derived from the LOAEL TRV by applying an uncertainty factor of 5.

14.2.2.2 Fish Eggs

The selected TRVs were also used in the LPRSA BERA (Windward 2019) and the draft LPR FFS (Battelle 2007). Three acceptable toxicity studies for three fish species reported the effects of methylmercury on the reproduction, behavior, physiology, and survival of fish eggs. These data, however, were not sufficient to create an SSD. The lowest LOAEL of 0.06 mg/kg ww was selected as the TRV and was the concentration in channel catfish eggs associated with a 48% survival at hatching and 30% survival at 4 days post-hatching (Birge et al. 1979). No NOAEL was reported in this study, so a NOAEL TRV of 0.0006 mg/kg ww was extrapolated from the LOAEL using a factor of 10.

14.2.2.3 Fish Diet

The selected TRVs were derived in the LPRSA BERA (Windward 2019), which Windwarddeveloped an SSD for methylmercury based on 15 LOAELs ranging from 0.0015 to 2.5 mg/kg bw/day in 10 species of fish reported in 13 studies. The 5th percentile (0.0056 mg/kg bw/day) was selected as the LOAEL TRV. A NOAEL TRV was estimated from the LOAEL using an extrapolation factor of 10. The LPR FFS (USEPA 2014) did not develop methylmercury fish dietary TRVs.

14.3 Birds

14.3.1 Toxicity Profile

In laboratory studies, adverse effects on the reproduction, growth, survival, and behavior were observed in birds as a result of dietary exposure to mercury. Specifically, the effects included reduced egg production, altered behavior of offspring, altered avoidance response, altered motivation to hunt prey, altered thermoregulation, and altered learning response behaviors in mallard ducks, young great egrets (*Ardea alba*), Japanese quails, zebra finches (*Taeniopygia guttata*), bobwhite quails, pigeons, and American kestrels (Heinz 1974, 1975, 1976, 1979; Hill and Soares 1987; Peakall and Lincer 1972). Chronic effects on birds of dietary mercury exposure included adverse effects on growth, development, reproduction, metabolism, and behavior (Eisler 2000).

14.3.2 TRVs

Table D-52 summarizes the bird TRVs used in the assessment, and the sections below describe how they were derived.

Table D-52 Bird Methylmercury TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	0.0096	0.096	Windward 2019 (six species SSD)	1	a, b
		0.013	0.026	Heinz 1974, 1975, 1979 (mallard duck reproduction)	3	c
Bird egg	mg/kg ww	0.18	1.8	Heinz 1974, 1976, 1979; Heinz and Hoffman 2003; (mallard duck reproduction)	1, 2	b, c

Notes:
KU = Key Uncertainty
a = TRV based on an SSD
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10
c = TRV based on a few studies

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

14.3.2.1 Bird Diet

The selected TRVs were derived in the LPRSA BERA (Windward 2019) where 11 studies on six species of birds that evaluated the effects of growth, reproduction, and mortality from methylmercury exposure were accepted to develop an SSD. LOAELs ranged from 0.064 to 8.78 mg/kg bw/day, and the 5th percentile of the SSD of 0.096 mg/kg bw/day was selected as the LOAEL TRV. The NOAEL TRV was estimated from the LOAEL using an extrapolation factor of 10.

The LPR FFS (USEPA 2014) selected LOAEL and NOAEL TRVs of 0.026 and 0.013 mg/kg bw/day, respectively, based on mallard duck reproduction data from Heinz (1974, 1975, 1979). The LOAEL TRV was derived from the reported LOAEL through the application of uncertainty factor of three that was used as an interspecies extrapolation factor, assuming mallards are three times less sensitive than the selected avian species evaluated.

14.3.2.2 Bird Eggs

Effects of mercury exposure measured in bird eggs were available from four studies all conducted on mallard ducks (Heinz 1974, 1976, 1979; Heinz and Hoffman 2003). The selected LOAEL TRV of 1.8 mg/kg ww represents the geometric mean of the five reported reproduction LOAELs where effects included embryo development, offspring survival, hatchability, avoidance response behavior, and egg/young production (Heinz 1974, 1976, 1979; Heinz and Hoffman 2003). The NOAEL TRV was estimated from the LOAEL TRV using a factor of 10. The LPR FFS (USEPA 2014) did not develop egg based TRVs for birds.

14.4 Mammals

14.4.1 Toxicity Profile

Exposure of mammals to mercury has been reported to adversely affect reproduction, growth, development, behavior, blood and serum chemistry, motor coordination, vision, hearing, histology, and metabolism (Eisler 2000). Adverse effects on growth, reproduction, behavior, and survival have been observed in mammals after dietary mercury exposure. These effects included a reduction in growth in lab rats and mink (Verschuuren et al. 1976) and significantly reduced growth and increased mortality in mink (Wobeser et al. 1976b; Aulerich et al. 1974). In addition, various studies have noted other effects, including increased adult mortality, depressed growth, altered offspring behavior, reduced whelping success, reproductive effects, changes to blood and serum chemistry, and decreased motor coordination in mink and rats (Dansereau et al. 1999; Hughes and Annau 1976; Aulerich et al. 1974; Verschuuren et al. 1976; Wobeser et al. 1976a,1976b; Schroeder and Mitchener 1975).

14.4.2 TRVs

Table D-53 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-53 Mammal Methylmercury TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	0.16	0.25	Wobeser et al. 1976b (mink growth and survival)	1	a
		0.016	0.027	Wobeser et al. 1976a, 1976b (mink growth and reproduction)	2	

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)
2 = LPR FFS (USEPA 2014)

The TRVs seclected were those derived in the LPRSA BERA (Windward 2019) and were based on the data reported by Wobeser et al. (1976b); although, two other mink studies were also evaluated. The LOAEL of 0.25 mg/kg bw/day was based on the growth and survival of mink following exposure to methylmercury in their diet for 93 days (Wobeser et al. 1976b). These TRVs were calculated using the study endpoints and assuming a body weight of 1.34 kg and a FIR of 0.18 kg/day based on Bleavins and Aulerich (1981). There is uncertainty associated with the limited number of dietary studies identified from the literature review.

The LPR FFS (USEPA 2014) developed LOAEL and NOAEL TRVs of 0.027 and 0.016 mg/kg bw/day, respectively, also based on mink the mink study by Wobeser et al. (1976b) as well as the study by Wobeser et al. (1976a). These TRVs differed from those developed for the LPRSA BERA because: 1)

the endpoints were growth and reproduction, 2) different body weight (1 kilogram) and FIR (0.15 kg/day) from Bleavins and Aulerich (1981) and Hornshaw et al. (1983), respectively, and 3) a subchronic to chronic factor of 10 was applied to the NOAEL and LOAEL.The application of uncertainty factors to TRVs is a primary source of uncertainty in these TRVs.

15 NICKEL

Nickel is a hard, silvery-white, naturally occurring metal that combines well with other metals (e.g., iron, copper, chromium, and zinc) to form mixtures called alloys, which are used in making metal coins, jewelry, and industrial equipment. Most nickel, however, is used to make stainless steel. Nickel is primarily found in the environment combined with oxygen or sulfur as oxides or sulfides. It is released during nickel mining and by industries that make or use nickel, nickel alloys, or nickel compounds, such as oil-burning power plants, coal-burning power plants, and trash incinerators (ATSDR 2005b).

In soil or sediment, nickel strongly attaches to particles containing iron or manganese. Under acidic conditions, nickel is more mobile in soil and might seep into groundwater. Nickel does not appear to concentrate in fish. Studies show that some plants can take up and accumulate nickel. However, it has been shown that nickel does not accumulate in small animals living on land that has been treated with nickel-containing sludge (ATSDR 2005b).

A number of animal studies have assessed the toxicity of nickel following oral exposure. Significant decreases in body and organ weights (liver, kidney, pituitary) were consistently observed in rats exposed to nickel chloride (American Biogenics Corporation 1988; Research Triangle Institute 1988a,1988b), nickel acetate (Whanger 1973), or nickel sulfate (Dieter et al. 1988). Other systemic effects included kidney damage and adverse lung effects at (American Biogenics Corporation 1988; Research Triangle Institute 1988b). However, the primary targets of toxicity appear to be to the respiratory tract following inhalation exposure; the immune system following inhalation, oral, or dermal exposure; and the reproductive system and the fetus following oral exposure. The most consistently reported adverse effects resulting from exposure to nickel are contact dermatitis and respiratory effects, including cancer (ATSDR 2005b; Eisler 2000). More specific ecotoxicity information is provided below by receptor group.

15.1 Benthic Invertebrates

15.1.1 Toxicity Profile

Adverse effects of nickel on aquatic invertebrates observed in laboratory studies include inhibited reproduction of daphnids, reduced growth in northern quahog (*Mercenaria mercenaria*), impaired reproduction and growth in water fleas, and abnormal development of sea urchin embryos (NRCC 1981; WHO 1991; Calabrese et al. 1977; Outridge and Scheuhammer 1993).

15.1.2 TRVs

Table D-54 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-54 Benthic Invertebrate Nickel TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	0.1	1.1	Borgmann et al. 2001 (amphipodsurvival)	1	a,b

Notes:
[1] = Total TEQ refers to total dioxin/furan TEQ, total PCB TEQ, and total PCB and dioxin/furan TEQ
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Source:
1 = LPRSA BERA (Windward 2019)

The nickel TRV for invertebrates was derived from a study by Borgmann et al. (2001) and were also used in the LPRSA BERA (Windward 2019). This study exposed the amphipod *Hyallela azteca* to nickel-spiked field-collected sediments for 28 days and reported mortality. The LOAEL of 1.1 mg/kg ww (assuming 80% moisture) associated with a 75% increase in mortality was selected as the LOAEL TRV. The proposed NOAEL TRV of 0.10 mg/kg ww (assuming 80% moisture) also came from the same study. An uncertainty specifically related to this study was the use of field-collected sediments with pre-spiked sediment chemistry that was not reported. The presence of sediment contaminants other than nickel could have played a role in the observed effects.

15.2 Fish

15.2.1 Toxicity Profile

Nickel accumulates in fish tissues and causes alterations in gill structure, including hypertrophy of respiratory and mucus cells, separation of the epithelial layer from the pillar cell system, cauterization and sloughing, and necrosis of the epithelium (Nath and Kumar 1989; Ellgaard et al. 1995; Ghazaly 1992; Evans et al. 1990). Sublethal effects include altered immunoregulatory mechanisms in tissues of the rainbow trout (Bowser et al. 1994) and reduced growth of rainbow trout (NRCC 1981; WHO 1991; Outridge and Scheuhammer 1993).

15.2.2 TRVs

Table D-55 summarizes the fish TRVs used in the assessment, and the section below describes how they were derived.

Table D-55 Fish Nickel TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish diet	mg/kg bw/day	0.14	1.4	Javed 2013 (Indian carp [*Labeo catla*] growth)	1	a, b

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10.

Source:
1 = LPRSA BERA (Windward 2019)

The selected TRVs were derived in the LPRSA BERA (Windward 2019) based on the review of three acceptable studies for nickel dietary toxicity in fish. The lowest LOAEL of 1.4 mg/kg bw/day was selected as the TRV and was associated with decreased growth in Indian carp over 12 weeks (Javed 2013). Because a NOAEL was not reported in this study, it was estimated using an extrapolation factor of 10. The reported food ingestion rate in the study was very low (0.18 to 0.19% bw/day), and to convert to a dietary dose, a FIR was assumed to be 2% bw/day. The LPR FFS (USEPA 2014) did not develop TRVs based on fish diet.

15.3 Birds

15.3.1 Toxicity Profile

Adverse effects of nickel on birds include metabolic upset, altered bone densities, inhibited growth and reduced survival in mallard ducks (Eisler 2000), decreased growth and survival, and increased nickel concentrations in bone and kidney in domestic chickens (Ling and Leach 1979). Chick embryos receiving injected doses of nickel had increased mortality (Ridgway and Karnofsky 1952) and disrupted glucose metabolism (Nielsen 1977).

15.3.2 TRVs

Table D-56 summarizes the bird TRVs used in the assessment, and the section below describes how they were derived.

Table D-56 Bird Nickel TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	15	33	Weber and Reid 1968 (chicken growth)	1	a

Notes:
[1] = Total TEQ refers to total dioxin/furan TEQ, total PCB TEQ, and total PCB and dioxin/furan TEQ
KU = Key Uncertainty
a = TRV based on a single study

Source:
1 = LPRSA BERA (Windward 2019)

The selected TRVs were derived in the LPRSA BERA (Windward 2019) and based on three acceptable studies for dietary nickel TRV derivation for birds. The lowest LOAEL of 33 mg/kg bw/day was selected as the TRV and was based on a study showing reduced growth in chickens after a 4-week exposure to nickel in the diet (Weber and Reid 1968). This LOAEL resulted in a 31% decrease in body weight compared to the control, and the NOAEL of 15 mg/kg bw/day came from the same study. The LPR FFS (USEPA 2014) did not develop TRVs for nickel.

15.4 Mammals

15.4.1 Toxicity Profile

Nickel-contaminated drinking water has adverse effects on rat reproduction and diets containing nickel carbonate, nickel chloride, or nickel sulfate cause reduced growth, disruptions of food intake and thyroid function, and emphysema and pneumonia in dogs, mice, or rats (Eisler 2000). Adverse effects of dietary exposure to nickel in rat, mouse, and dog laboratory studies include decreased body weight (Ambrose et al. 1976; Nation et al. 1985; Weber and Reid 1969), an increase in the number of stillborn young (Ambrose et al. 1976), and a decrease in the number of pups surviving to weaning (Ambrose et al. 1976; Weber and Reid 1969).

15.4.2 TRVs

Table D-57 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-57 Mammal Nickel TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	40	80	Ambrose et al. 1976 (rat reproduction)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Source:
1 = LPRSA BERA (Windward 2019)

The TRVs selected are the same as those used by LPRSA BERA (Windward 2019). Three acceptable studies were evaluated and the lowest LOAEL of 80 mg/kg bw/day was selected, which was based on reduced body weight of rat offspring over three generations (Ambrose et al. 1976). The NOAEL from this study was 40 mg/kg bw/day and was also selected as a TRV (Ambrose et al. 1976). The LPR FFS (USEPA 2014) did not develop nickel TRVs.

16 SELENIUM

Selenium is a naturally occurring metal found in air, water, sediment and soil. It may be released from natural sources (e.g., leaching and weathering of rocks, volcanic eruptions) or anthropogenic sources (e.g., manufacturing/production of rubber, metal alloys, textiles, fungicides; or burning of coal, oil, and solid waste) (USEPA 2007c). Selenium is essential for growth in plants and is an essential trace element in animals. Selenium toxicity is associated with reproductive and developmental effects in wildlife (USEPA 2007c).

The behavior of selenium in the environment is influenced by its oxidation state, which is dependent on ambient conditions, including pH, oxidation/reduction potential, and biological activity (ATSDR 2003). In surface water and sediments/soil, it is expected to be found as the salts of selenic and selenious acids. It bioaccumulates in aquatic organisms and, in some cases, may biomagnify (ATSDR 2003).

Elevated concentrations of selenium, above nutritional requirements, in diet or water were associated with growth retardation; reproductive failure and reduced hatching; and reproductive abnormalities, including congenital malformations, lowered survival, and histopathologies in liver, kidney, liver, heart, and gills (Eisler 2000). More specific ecotoxicity information is provided below by receptor group.

16.1 Benthic Invertebrates

16.1.1 Toxicity Profile

Selenite is more toxic than selenate and is preferentially concentrated over selenate by mussels (*Mytilus galloprovincialis*) (Measures and Burton 1980). Ninety-six-hour toxicity tests found LC50 values of 710 ppb for *Daphnia magna* (Halter et al. 1980) and 24,000 ppb for *Physa* sp. snails (Reading 1979). Waterborne selenium toxicity data revealed a broad range of sensitivity among taxa, with acutely (1- to 4-day test duration) toxic water concentrations spanning more than 3 orders of magnitude. *Hyalella* (Amphipoda) was the most sensitive taxon and *Nephelopsis* (Hirudinea) was the most tolerant (deBruyn and Chapman 2007). Lethal and sublethal toxic effects were observed at somewhat lower water concentrations in laboratory tests of longer duration and at much lower water concentrations in experimental streams for *Hyalella* sp. (deBruyn and Chapman 2007). Exposure to selenium in water impaired the development of *Chironomus* and *Caecidotea* (Isopoda) and reduced abundance in *Tubifex* (Tubificidae) (deBruyn and Chapman 2007). Selenium exposure in water caused reduced growth rates in the midge (*Chironomus decorus*) (Malchow et al. 1995).

16.1.2 TRVs

Table D-58 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-58 Benthic Invertebrate Selenium TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	0.05	0.51	Malchow et al. 1995 (midge; growth)	1	a

Notes:
KU = Key Uncertainty

a = TRV based on a single study

Source:
1 = LPRSA BERA (Windward 2019)

The selected TRVs were derived from a study by Malchow et al. (1995) and were also used in the LPRSA BERA (Windward 2019). Malchow et al. (1995) exposed midges to selenate in the diet for 96 hrs and reported effects on growth. The LOAEL from this study, a tissue concentration of 0.51 mg/kg ww, represents a 15% decrease in growth, which was statistically significant relative to the control. The NOAEL from the same study was 0.05 mg/kg ww. Both the LOAEL and NOAEL from this study were selected as TRVs. There is uncertainty in the potential for population-level impacts to result from a decreased growth of 15% (Vandermeer and Goldberg 2003) and also uncertainty that the LOAEL tissue concentration is associated with adverse effects given that tissue concentrations measured at 48 hrs were up to 0.89 mg/kg ww yet showed no adverse effects on growth, and aquatic invertebrate background tissue concentrations are reported to range from 0.40 to 4.5 mg/kg dw (U.S. Department of the Interior 1998). These uncertainties suggest the selected TRVs may overestimate the potential for adverse effects in invertebrates based on selenium tissue concentrations.

16.2 Fish

16.2.1 Toxicity Profile

All embryos of the zebrafish survived exposure to 3,000 ppb of selenium during development, but more than 90% of the resultant larvae died soon after hatching. At 1,000 ppb, survival was similar to that in controls (Niimi and LaHam 1975). Failed reproduction and population declines were found in green sunfish (*Lepomis cyanellus*) from a lake in North Carolina receiving selenium (as fly ash wastes from a coal-fired power station). The selenium levels were elevated in the liver and other tissues; kidney, heart, liver, and gills showed histopathology; and the blood chemistry was altered. Ovaries of these fish had numerous necrotic and ruptured egg follicles that may have contributed to the population extinction (Sorensen et al. 1984). In laboratory tests, eggs of common carp (*Cyprinus carpio*) hatched normally when incubated in media containing 5,000 ppb of selenium (Huckabee and Griffith 1974), as did eggs of lake trout (*Salvelinus namaycush*) at 10,000 ppb of selenium (Klaverkamp et al. 1983). Exposure to selenium was associated with anemia and reduced hatchlings (Hodson et al. 1980), reduced growth in rainbow trout fry (Adams 1976), increased polyploid cells, and some deaths in the edible goby (*Boleophthalmus dussumieri*) (Krishnaja and Rege 1982).

16.2.2 TRVs

Table D-59 summarizes the fish TRVs used in the assessment, and the sections below describe how they were derived.

Table D-59 Fish Selenium TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	Not derived	1.6	Coyle et al. 1993; Hermanutz et al. 1992; Ogle and Knight 1989 (Bluegill, sunfish, fathead minnow; reproduction)	1	a
Fish diet	mg/kg bw/day	0.011	0.11	Windward 2019 (7 species SSD)	1	b

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = TRV based on an SSD

Source:
1 = LPRSA BERA (Windward 2019)

16.2.2.1 Fish Whole-Body Tissue

The selected TRVs were derived in the LPRSA BERA (Windward 2019); there was a lack of sufficient whole-body LOAEL data to derive an SSD. The LOAEL TRV of 1.6 mg/kg ww was selected,which is the EC10 for maternal whole-body concentrations of the most sensitive species (bluegill sunfish and fathead minnow) evaluated by DeForest and Adams (2011) and associated with larval mortality or edema. Given the LOAEL represented an EC10 below which no adverse effects were expected, a NOAEL TRV was not defined. No TRVs were available in the LPR FFS (USEPA 2014) for selenium in fish tissue.

16.2.2.2 Fish Diet

The selected TRVs were those derivd in the LPRSA BERA (Windward 2019) which developed an SSD from eight dietary studies of selenium in fish, examining growth, reproduction, and mortality. These studies reported nine LOAELs for selenium ranging from 0.19 to 1.2 mg/kg bw/day in seven species of fish (Chinook salmon, rainbow trout, bluegill, Sacramento splittail [*Pogonichthys macrolepidotus*], striped bass, white sturgeon, and fathead minnow). The LOAEL TRV (0.11 mg/kg bw/day), represents the 5th percentile, which is less than the lowest measured LOAEL reported in the literature. A NOAEL TRV was estimated from the LOAEL using an extrapolation factor of 10. There were not selenium dietary fish TRVs developed in the LPR FFS (USEPA 2014).

16.3 Birds

16.3.1 Toxicity Profile

Embryos of the domestic chicken are extremely sensitive to selenium. Hatchability of domestic chicken eggs was reduced by concentrations of selenium in feeds (6 to 9 ppm) that were too low to produce poisoning in other avian species. Adverse effects of dietary exposure to selenium were associated with decreased egg weight, decreased egg production and hatchability, anemia, elevated kidney selenium residues in chicks, and a high incidence of grossly deformed embryos with missing or distorted eyes, beaks, wings, and feet (Ort and Latshaw 1978; Harr 1978). Selenomethionine was more effective than sodium selenite in raising the selenium content of tissues and eggs (Moksnes 1983).

Ohlendorf and Harrison (1986) reported severe reproductive effects in ducks (*Anas* spp.), American coots, and other species of aquatic birds nesting at irrigation drainwater ponds in the San Joaquin Valley, California, which contained high concentrations of selenium at approximately 300 ppb. Of 347 nests examined from this site, approximately 40% had at least one dead embryo and approximately 20% had at least one embryo or chick with obvious external anomalies, including missing or abnormal beaks, eyes, wings, legs, or feet. In addition, brain, heart, liver, and skeletal anomalies were recorded.

Heinz et al. (1987; 1989) evaluated the effects of dietary selenium on mallard duck reproduction. Ducks given diets containing 100 ppm of inorganic selenite usually died within a month and exhibited reduced food intakes and significant weight loss.

16.3.2 TRVs

Table D-60 summarizes the bird TRVs used in the assessment, and the section below describes how they were derived.

Table D-60 Bird Selenium TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	0.42	0.82	Heinz et al. 1989 (mallard duck reproduction)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Source:
1 = LPRSA BERA (Windward 2019)

The selected TRVs were derived in the LPRSA BERA (Windward 2019) where six studies were acceptable for the development of TRVs for selenium toxicity in birds. The lowest of these LOAELs, 0.82 mg/kg bw/day, was selected as the LOAEL TRV based on a study that exposed mallard ducks to selenium in the diet for 100 days (Heinz et al. 1989). At this LOAEL, there was a significant effect on offspring growth and survival compared to the control. The NOAEL of 0.42 mg/kg bw/day came from the same study and was selected as the NOAEL TRV. The TRVs derived from this study are the same as

those reported by Sample et al. (1996). Bird selenium TRVs were not developed in the LPR FFS (USEPA 2014).

16.4 Mammals

16.4.1 Toxicity Profile

Selenosis caused congenital malformations, reduced reproduction, and high offspring mortality in rats, mice, swine (*Sus scrofa domesticus*), and cattle (Harr 1978; National Research Council 1983). In rats, selenium did not induce cirrhosis or neoplasia; however, intestinal lesions were observed during lifetime exposure to selenium (Harr 1978; National Research Council 1983). Yonemoto et al. (1983) demonstrated that some selenotoxic effects in mice, including abortion and maternal death, were prevented by prior treatment with vitamin E.

16.4.2 TRVs

Table D-61 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-61 Mammal Selenium TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	0.016	0.16	Behne et al. 1992 (rat growth)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Source:
1 = LPRSA BERA (Windward 2019)

The LPRSA BERA (Windward 2019) developed TRVs based on the review of four accepted studies and selected the lowest LOAEL (0.16 mg/kg bw/day), which was based on a decrease in the body weights of rats exposed to dietary selenomethionine (Behne et al. 1992). Because the study did not have a NOAEL it was estimated from the LOAEL using an uncertainty factor of 10 resulting in a TRV of 0.016 mg/kg bw/day. There is uncertainty associated with the limited number of dietary studies identified from the literature review. There is also uncertainty associated with the use of an extrapolation factor to derive a NOAEL. The LPR FFS did not develop a mammal diet TRV for selenium (USEPA 2014).

17 SILVER

Photographic materials and mining are the major anthropogenic sources of silver released into the environment (ATSDR 1990). It is also released naturally by the breakdown of silver-bearing rocks and soil by wind and rain. Silver may biomagnify in some aquatic invertebrates (Adriano 1986), and it is highly toxic to aquatic organisms (Eisler 2000). Elevated concentrations can cause larval mortality, developmental abnormalities, and reduced larval growth in fish; growth reduction in juvenile mussels (Calabrese et al. 1984); and adverse effects on reproduction in gastropods (Nelson et al. 1983). Silver is toxic to soil microbes, thus inhibiting biotransformation (ATSDR 1990). Effect of silver exposure on aquatic organisms include inhibition of reproduction and histopathologies in major organ systems, and effects on birds and mammals include pulmonary edema, congestion, and mortality (Eisler 2000). More specific ecotoxicity information is provided below by receptor group.

17.1 Benthic Invertebrates

17.1.1 Toxicity Profile

Aquatic insects concentrate silver in relative proportion to environmental levels (Nehring 1976). Marine gastropods exposed to silver exhibited inhibited reproduction (Nelson et al. 1983) and juvenile Pacific oysters (*Crassostrea gigas*) had high silver accumulations in tissues and a reduced capacity to store glycogen (Berthet et al. 1990). Grass shrimp incorporate silver dissolved in brackish water but not from planktonic or detrital food sources containing elevated silver burdens (Connell et al. 1991). Variations in the ability of decapod crustaceans to accumulate silver are potentially due to differences in hepatopancreas morphology, with bioconcentration factors ranging from 70 to 4,000 (Pouvreau and Amiard 1974). The hepatopancreas, or digestive gland, is the major repository of silver in decapods (Greig 1979; Greig et al. 1977). Whole-body bioconcentration factors of silver in three species of aquatic insects ranged from 21 to 240 in water during exposure of 3 to15 days. In bluegill sunfish (*Lepomis macrochirus*), this value was less than 1 after exposure for 28 days (USEPA 1980b). The marine gastropod (*Crepidula fornicata*) exposed to silver in water showed histopathology and inhibited reproduction (Nelson et al. 1983). Molt frequency of a mayfly (*Isonychia bicolor*) was a sensitive indicator of silver stress over time (Diamond et al. 1990). Other adverse effects include reduced growth rates in Eastern oysters and mussels (Berthet et al. 1992, Sanders et al. 1990) and inhibition of embryonic development in mussels (Bryan and Langston 1992).

17.1.2 TRVs

Table D-62 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-62 Benthic Invertebrate Silver TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	0.49	0.59	Naddy et al. 2007 (Daphnia growth)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Source:
1 = LPRSA BERA (Windward 2019)

The only study found acceptable for the derivation of a TRV was Naddy et al. (2007). This study exposed the cladoceran to water-based silver for 7 days and examined the effects of growth and reproduction. This study determined a LOAEL of 0.59 mg/kg ww and a NOAEL of 0.49 mg/kg ww that was associated with reduced growth and reproduction. Both were accepted as TRVs and were also used in the LPRSA BERA (Windward 2019).

17.2 Fish

17.2.1 Toxicity Profile

Silver ion (Ag+) is reportedly the most toxic chemical species of silver to fishes. Silver ion was 300 times more toxic than silver chloride to fathead minnows, 15,000 times more toxic than silver sulfide, and more than 17,500 times more toxic than silver thiosulfate complex. In all cases, toxicity reflected the free silver ion content of tested compounds (LeBlanc et al. 1984). A similar pattern was noted in rainbow trout (Hogstrand et al. 1996). Silver was less toxic to fathead minnows under conditions of increasing water hardness between 50 and 250 milligrams CaCO3/L, which increased the pH between 7.2 and 8.6. Eggs of rainbow trout exposed to silver had increased embryotoxicity and hatched prematurely; resultant fry had a reduced growth rate (Davies et al. 1978). Accumulation of silver in largemouth bass and bluegills increased with increasing concentrations of ionic silver and increasing duration of exposure (Coleman and Cearley 1974). The liver is usually considered the major repository of silver in fish (Garnier et al. 1990).

17.2.2 TRVs

Table D-63 summarizes the fish TRVs used in the assessment, and the sections below describe how they were derived.

Table D-63 Fish Silver TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	0.11	0.24	Guadagnolo et al. 2001 (rainbow trout mortality)	1	a
Fish diet	mg/kg bw/day	70	Not derived	Galvez and Wood 1999 (rainbow trout growth)	2, 3	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Sources:
1 = LPRSA BERA (Windward 2019)
2 = TRV derived for the NBSA BERA
3 = LPRSA BERA (Windward 2019) Appendix A3-1

17.2.2.1 Fish Whole-Body Tissue

The selected TRVs were developed in the LPRSA BERA (Windward 2019) where only one study examining effects on survival to meet TRV acceptability criteria was found. Guadagnolo et al. (2001) exposed embryonic rainbow trout to aqueous silver for 32 days and determined a mortality LOAEL of 0.24 mg/kg ww and a NOAEL of 0.11 mg/kg ww. Both were selected as TRVs. An uncertainty in this study was that tissue burdens did not consistently correlate with mortality; therefore, adverse effects were not dependent on tissue concentrations. The LPR FFS (USEPA 2014) did not develop TRVs for silver.

17.2.2.2 Fish Diet

Neither the LPRSA BERA nor the LPR FFS developed dietary TRVs for fish exposed to silver. For the NBSA BERA, the TRV was derived from the study by Galvez and Wood (1999) who exposed rainbow trout to silver in the diet for 58 days and found no adverse effects on growth at 70 mg/kg bw/day, which was accepted as the NOAEL TRV. A LOAEL was not available from this study, which adds to the uncertainty of evaluating risk based on an unbounded NOAEL.

17.3 Birds

17.3.1 Toxicity Profile

Signs of chronic silver ion intoxication in tested birds included cardiac enlargement, vascular hypertension, hepatic necrosis, anemia, lowered immunological activity, altered membrane permeability, kidney pathology, enzyme inhibition, growth retardation, and a shortened life span (Smith and Carson 1977; Freeman 1979; ATSDR 1990).

Turkey poults (*Meleagris gallopavo*) on diets containing silver had enlarged hearts and reduced growth, hemoglobin, and hematocrit (USEPA 1980b). Chicken eggs injected with silver nitrate had a 50% reduction in survival but no developmental abnormalities (Ridgway and Karnofsky 1952). Growth

suppression and liver necrosis were adverse effects of silver on chicks (Smith and Carson 1977). Chicks on copper and vitamin E-deficient diets experienced reduced growth when given drinking water or food containing silver (Smith and Carson 1977).

17.3.2 TRVs

Table D-64 summarizes the bird TRVs used in the assessment, and the section below describes how they were derived.

Table D-64 Bird Silver TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	9.86	98.6	USEPA 2006b (mallard duck mortality)	1	a, b

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = LOAEL estimated from a NOAEL with an extrapolation factor of 10.

Source:
1 = TRV derived for the NBSA BERA

Neither the LPRSA BERA (Windward 2019) nor the LPR FFS (USEPA 2014) developed bird dietary TRVs for silver. Therefore, the selected TRVs were derived specifically for the NBSA site based on the study by Van Vleet (1977) as cited in the EcoSSL for silver (USEPA 2006b). The LOAEL of 98.6 mg/kg bw/day was reported as a mortality LOAEL following three weeks of dietary exposure of juvenile mallards (USEPA 2006b). This study did not report a NOAEL thus, the NOAEL TRV was estimated from the LOAEL using an extrapolation factor of 10.

17.4 Mammals

17.4.1 Toxicity Profile

Studies with small laboratory mammals show that long-term exposure to high levels of silver nitrate in drinking water may result in sluggishness and enlarged hearts (ATSDR 1990), kidney damage, impaired conditioned-reflex activities, immunological resistance, and altered brain nucleic acid content (USEPA 1980b). The extent of absorption of an administered dose of silver depends on silver speciation, the presence and extent of silver-binding proteins, and other variables.

Sublethal effects include brain histopathology in rabbits, kidney damage in rats, sluggishness in mice, reduce growth in guinea pigs, and high accumulations in the kidneys and liver and liver necrosis in rats (ATSDR 1990; USEPA 1980b).

17.4.2 TRVs

Table D-65 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-65 Mammal Silver TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	18.8	188	Shavlovski et al. 1995 (rat reproduction); cited in USEPA 2006b	1	a,b

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Source:
1 = TRV derived for the NBSA BERA

The silver LOAEL TRV of 188 mg/kg bw/day was derived from the USEPA (2006b) Silver Eco SSL report and, specifically, the study by Shavlovski et al. (1995), which reported reproductive effects on rats. A NOAEL was estimated using a factor of 10 applied to the LOAEL. This was the only study accepted by USEPA for the reproduction endpoint. There is uncertainty with only having a single TRV, a LOAEL, as the basis of the assessment. Neither the LPRSA BERA (Windward 2019) nor the LPR FFS (USEPA 2014) developed mammal dietary TRVs for silver.

18 ZINC

Zinc is one of the most common elements in the Earth's crust. It is used for a variety of industrial purposes, including as a coating for iron or other metals to prevent rust and corrosion or mixed with other metals to form alloys, such as brass and bronze. Zinc sulfide and zinc oxide are used to make white paints, ceramics, rubber, and other products. Zinc compounds are used to preserve wood, to manufacture and dye fabrics, and by the drug industry in common products, such as vitamin supplements, sun blocks, deodorants, skin preparations, and anti-dandruff shampoos (ATSDR 2005c).

Zinc enters the air, water, and soil as a result of both natural processes and human activities. Zinc is an essential nutrient to animals, but elevated exposure levels can be toxic to many types of plants and animals, where growth, survival, and reproduction can all be adversely affected (Eisler 2000). In aquatic systems, zinc tends to be partitioned into sediment and less frequently dissolved as hydrated zinc ions and organic and inorganic complexes (MacDonald 1993). Elevated zinc levels can cause mortality, pancreatic degradation, reduced growth, and decreased weight gain in birds (Eisler 2000; NAS 1980). Elevated zinc concentrations can cause a wide range of problems in mammals' cardiovascular, developmental, immunological, neurological, hematological, and reproductive systems as well as target organs, including the pancreas, liver, and kidney (Eisler 2000). More specific ecotoxicity information is provided below by receptor group.

18.1 Benthic Invertebrates

18.1.1 Toxicity Profile

Molluscs tend to accumulate zinc far in excess of the organism's immediate needs without negative impacts (Eisler 2000). Eastern oysters, for example, may naturally contain up to 4 g/kg soft parts, which is comparable to accumulations observed in oysters exposed to 0.2 mg/L for 20 weeks (NAS 1979). Zinc tends to accumulate in the molluscan digestive gland and stomach (Eisler 2000; Sprague 1986; Sullivan et al. 1988), the kidneys in mussels and scallops (Pectinidae), and the digestive gland in oysters (Sprague 1986). Zinc in molluscan tissues is usually elevated under conditions of increasing water temperature and pH and decreasing salinity (Eisler 2000) but can vary among species (Chu et al. 1990). Variations in zinc content of clam tissues were associated with seasonal changes in tissue weights (Cain and Luoma 1986). Unlike decapod crustaceans, marine amphipods do not regulate body zinc concentrations, and body burdens of zinc may reflect sediment total zinc levels (Rainbow et al. 1989).

Zinc was most toxic to molluscs at elevated temperatures (Eisler 1977; Sprague 1986; Khangarot and Ray 1987), in comparatively soft water or to marine molluscs in low salinity (Sprague 1986; Khangarot and Ray 1987), at earlier developmental stages (Munzinger and Guarducci 1988), at low dissolved oxygen concentrations (Khangarot and Ray 1987), and with increasing exposure to high zinc concentrations (Amiard et al. 1986). Toxicity was usually greatest to marine crustaceans and larvae (Eisler 1980).

Adverse effects of zinc to crustaceans include gill histopathology in prawns (*Macrobrachium hendersodyanum*) (Patel and Kaliwal 1989); increased tissue total proteins, decreased glycogen, and decreased acid phosphatase activity in crabs (*Portunus pelagicus*) (Hilmy et al. 1988); and reduction in

limb regeneration of fiddler crabs (Weis 1980). Freshwater insects, including many species of mayflies, damselflies, stoneflies, and caddisflies, are relatively tolerant to zinc, with LC50 values usually >1.33 mg/L – although some species were adversely affected at concentrations between 30 and 37 µg/L (USEPA 1987).

18.1.2 TRVs

Table D-66 summarizes the benthic invertebrate TRVs used in the assessment, and the section below describes how they were derived.

Table D-66 Benthic Invertebrate Zinc TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Benthic invertebrate whole-body tissue	mg/kg ww	5.1	51	Muyssen et al. 2006 (crustacean survival)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study
b = NOAEL estimated from a LOAEL with an extrapolation factor of 10

Source:
1 = LPRSA BERA (Windward 2019)

Zinc is an essential nutrient for invertebrates, and thus they have mechanisms to regulate their tissue burdens (Rainbow 2007). A whole-body zinc concentration of 6.9 mg/kg ww is considered to represent a level consistent with nutritional requirement (Rainbow 2007). Muyssen et al. (2006) reported a LOAEL of 51 mg/kg ww associated with reduced *D. magna* survival during a 21-day aqueous zinc exposure. This was the lowest chronic LOAEL for crustaceans that was greater than the zinc nutritional threshold and was selected as a TRV in the LPRSA BERA (Windward 2019). No NOAEL was available from this study; therefore, a NOAEL TRV (5.1 mg/kg ww) was extrapolated from the LOAEL TRV using an uncertainty factor of 10. There is uncertainty associated with the derivation of a NOAEL using an extrapolation factor.

18.2 Fish

18.2.1 Toxicity Profile

Freshwater fish are more sensitive to zinc than marine species, and embryos and larvae are the most sensitive developmental stages. Zinc toxicosis affects freshwater fish by destruction of gill epithelium and consequent tissue hypoxia. Signs of acute zinc toxicosis in freshwater fish include osmoregulatory failure, acidosis and low oxygen tensions in arterial blood, and disrupted gas exchange at the gill surface and at internal tissue sites (Spear 1981). Zinc poisoning caused fish to swim at the surface, be lethargic and uncoordinated, hemorrhage at the gills and base of fins, shed scales, and exude extensive body and gill mucous (Bengeri and Patil 1986). Acute zinc poisoning in fish is generally caused by blocking gas exchange across the gills, causing hypoxia at the tissue (Burton et al.1972; NAS 1979; Everall et al. 1989; Grobler et al. 1989). Cardiorespiratory responses to zinc in the spangled perch (*Leiopotherapon*

unicolor) are similar to those induced by hypoxia. Zinc-poisoned perch had damaged gill epithelia, resulting in impaired gas exchange and lowered oxygen tension in arterial blood (Gehrke 1988). Acute exposures to high-lethal concentrations of zinc also caused histopathology of epithelia lining the oral capacity (Eisler 2000).

18.2.2 TRVs

Table D-67 summarizes the fish TRVs used in the assessment, and the sections below describe how they were derived.

Table D-67 Fish Zinc TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Fish whole-body tissue	mg/kg ww	287	403	Pierson 1981 (guppy growth)	1	a
Fish diet	mg/kg bw/day	19	38	Takeda and Shimma 1977 (rainbow trout growth)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Source:
1 = LPRSA BERA (Windward 2019)

18.2.2.1 Fish Whole-Body Tissue

The selected TRVs eere derived in LPRSA BERA (Windward 2019) where four studies were found to be acceptable to derive fish tissue TRVs for zinc. Zinc is an essential nutrient for fish. Nutritional thresholds for fish in the literature range from 10 – 100 mg/kg ww (Sun and Jeng 1998; Schmitt and Brumbaugh 1990). The lowest LOAEL (403 mg/kg) that is also greater than the nutritional threshold, was selected as the TRV based on the study by Pierson (1981). This study exposed immature guppies to aqueous zinc for 134 days and the LOAEL was associated with reduced growth and reproduction. The NOAEL of 287 mg/kg ww came from the same study and was also selected as the TRV. The LPR FFS (USEPA 2014) did not derive TRVs for zinc in fish.

18.2.2.2 Fish Diet

The selected TRVs were derived in the LPRSA BERA (Windward 2019) and were based on the study by Takeda and Shimma (1977) who reported a 20% reduction of growth in rainbow trout at a dietary concentration of 38 mg/kg bw/day. This was used as the LOAEL TRV. The NOAEL of 19 mg/kg bw/day was identified in the same study and was also selected as the TRV. The food ingestion rate was not reported in this study, so the doses were estimated in the LPRSA BERA assuming an average rainbow trout feeding rate of 1.9% bw/day (Windward 2019). The LPR FFS (USEPA 2014) did not derive TRVs for zinc in fish.

18.3 Birds

18.3.1 Toxicity Profile

Zinc excess in avian species is associated with decreased body weight, gizzard and pancreatic lesions, and biochemical changes (WHO 2001) and can cause mortality, pancreatic degradation, reduced growth, and decreased weight gain in birds (Eisler 2000; NAS 1980). Adverse effects found in laboratory exposure studies include pancreatic degeneration in ducks, reduced growth in domestic chickens, and experienced pancreas histopathology when fed a selenium-deficient but zinc-adequate diet (Eisler 2000).

18.3.2 TRVs

Table D-68 summarizes the bird TRVs used in the assessment, and the section below describes how they were derived.

Table D-68 Bird Zinc TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Bird diet	mg/kg bw/day	82	124	Roberson and Schaible 1960 (chicken growth)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Source:
1 = LPRSA BERA (Windward 2019)

The selected TRVs for zinc were derived in the LPRSA BERA (Windward 2019) based on a review of six toxicity studies conducted with chickens and mallard ducks. A decrease in chick body weight by as much as 21% (compared to the control) was observed after exposure to zinc at a dietary dose of 124 mg/kg bw/day for five weeks (Roberson and Schaible 1960). This dietary dose was accepted as the LOAEL TRV. The next lowest dose of 82 mg/kg bw/day did not have a significant effect on growth and was accepted as the NOAEL TRV.

18.4 Mammals

18.4.1 Toxicity Profile

Zinc is an essential nutrient for regulating a number of metalloenzymes in animals (ATSDR 2005c). Absorption of zinc occurs in the intestine, particularly the duodenum (ATSDR 2005c). Following absorption by the intestine, zinc is rapidly distributed to the liver, kidneys, prostate, muscles, bones, and pancreas. Zinc can have negative effects on tissues; interfere with the metabolism of other ions (such as copper, calcium, and iron); inhibit erythrocyte production and function; and have cardiovascular, developmental, neurological, immunological, liver, and kidney effects (Eisler 2000; Domingo 1994; ATSDR 2005c; WHO 2001; European Chemicals Bureau 2004). Mammalian studies have shown

vomiting, depressed growth rate, purgation, and ataxia after exposure to excess zinc (Clarke et al. 1981; Friberg et al. 1986). Mammals are fairly tolerant of extended periods on diets containing >100 times the minimum daily zinc requirement. But excessive zinc through inhalation or ingestion harms mammalian survival, metabolism, and well-being (Eisler 2000).

18.4.2 TRVs

Table D-69 summarizes the mammal TRVs used in the assessment, and the section below describes how they were derived.

Table D-69 Mammal Zinc TRVs

Assessment	Unit	NOAEL	LOAEL	Study	Source Note	KU
Mammal diet	mg/kg bw/day	160	320	Schlicker and Cox 1968 (rat reproduction)	1	a

Notes:
KU = Key Uncertainty
a = TRV based on a single study

Source:
1 = LPRSA BERA (Windward 2019)

The selected TRVs were the same as those used in the LPRSA BERA (Windward 2019) and were derived from the study by Schlicker and Cox (1968). The LOAEL TRV (320 mg/kg bw/day) reduced fetal growth. The NOAEL from this study, 160 mg/kg bw/day, was also used as the TRV. The LPR FFS (USEPA 2014) did not derive TRVs for zinc in mammals.

19 TRV UNCERTAINTIES

This section discusses some of the key uncertainties regarding TRVs. TRV-related uncertainty is a key factor affecting the magnitude of risk estimates. Two primary means by which this assessment attempted to reduce uncertainty in the TRVs was by 1) using TRVs already accepted by USEPA in other regional assessments, and 2) quantifying the TRV uncertainty by calculating a range of HQs using multiple sets of TRVs. Two sets of TRVs available from regional ecological risk assessment were evaluated in the NBSA BERA:

1. TRVs developed for the LPRSA BERA (Windward 2019).
2. TRVs developed for the LPR FFS (USEPA 2014).

Use of consistent TRVs at these sites allows for comparison of risk estimates presented herein with those in the LPRSA BERA (Windward 2019) and LPR FFS (USEPA 2014). In some cases, TRVs were derived for COPECs unique to the NBSA, or TRVs were revised from values used in the LPR assessments to be more relevant to species in the NBSA (e.g., for marine species). However, the same TRV derivation approach was used herein as in these other assessments; thus, the inherent uncertainty is not expected to be substantially different from the inherent uncertainty associated with the TRVs used in the other assessments. In general, the USEPA acknowledges and GSH concurs that the LPR FFS TRVs are more conservative than comparable TRVs developed by the Cooperating Parties Group. The intent of using both TRV sources, when available, is to understand the potential range of effects within a particular trophic category from more sensitive to less sensitive endpoint receptors.

The potential for TRV uncertainty to affect the magnitude and direction (over- or under-estimation) of risk estimates can generally not be determined with the exception of the quantitative assessment of alternate TRVs, which has been previously discussed in the uncertainty sections for each specific receptor. Additionally, there is uncertainty related to COPECs with lacking or estimated TRVs. These specific sources of TRV uncertainty are discussed below.

19.1 COPECs with Limited Toxicity Data TRVs

Most of the TRVs are based on a single study that met the acceptability criteria for TRV development and, if several studies met these criteria, was the study with the lowest LOAEL and the highest NOAEL below the LOAEL. In most cases, if a study provided the basis for the NOAEL TRV, the NOAEL TRV was obtained from the same study as the LOAEL TRV. The fundamental uncertainty with this approach is the number of studies evaluated. Confidence increases and uncertainty decreases when more toxicological data are available for consideration. For COPECs with limited toxicity data, three things are likely: 1) toxicity information is lacking because those COPECs are comparatively not as toxic or bioaccumulative as COPECs for which large amounts of toxicological information are available (i.e., highly toxic compounds have been prioritized and investigated); 2) these COPECs likely have a smaller footprint at the site compared to the primary COPECs; and 3) the occurrence of the footprint of these COPECs likely overlaps with the presence of other contaminants. Given that this risk assessment determined that many of the COPECs present with known toxicity were found to be present at levels that do not pose adverse risk, it is also likely that the magnitude of risk for COPECs without TRVs is minimal.

19.2 Non-COPEC Pesticides Detected in Sediments and Biota

Additional organochlorine pesticides were detected in NBSA sediment and tissue samples, but were not included as COPECs, as they have limited ecotoxicological information available for them to establish TRVs. These include total BHC [alpha-, beta-, delta-, and gamma-], aldrin, and mirex. The uncertainty related to the potential for adverse effects from these compounds was qualitatively evaluated by examining the mode of action and relative toxicity as compared to pesticide COPECs for which there are TRVs and that were formally evaluated in the BERA, including: total chlordane (alpha-chlordane, gamma-chlordane, oxychlordane, cis-nonachlor, and trans-nonachlor), DDx, dieldrin, and hexachlorobenzene. In general, the potential toxicity of these compounds is within the range of the pesticide COPECs evaluated in the BERA, and none are considered as toxic as DDx (ATSDR 2002a, 2005a). As such, the risks from these compounds (based on the risk results for the BERA pesticide COPECs) are considered to be *de minimis*.

19.3 Unbounded TRVs and TRV Estimated with Extrapolation Factors

If possible, LOAEL and NOAEL TRVs were estimated from the same laboratory study. The NOAEL and LOAEL concentrations are an artifact of the exposure concentrations evaluated. The nature and magnitude of the effects, if any, that may occur between the LOAEL and NOAEL is unknown. There were several instances where only a LOAEL could be derived from a study, in which case NOAELs were estimated from these unbounded LOAELs using the well-accepted practice of applying an uncertainty factor of 10 based on USEPA guidance (USEPA 1997). Several of these LOAELs and estimated NOAELs were used in the LPRSA BERA (Windward 2019) and LPR FFS (USEPA 2014) assessments. An extrapolation factor of 10 for some chemicals may not accurately estimate the true factor difference between the LOAEL and NOAEL based on differences of dose response between chemicals. For example, where LOAELs and NOAELs were derived from the same study, the factor difference between these TRVs for mammals ranged from 2 to 499 with a median of 4. For inorganics, specifically, the median difference was 2. Thus, an extrapolation factor of 10 likely puts the estimated NOAEL below the true NOAEL in which case potential risks would be over-estimated.

In a few instances, COPEC TRVs were left unbounded, and the extrapolation factor applied to the known TRV was not used:

- Mammalian dietary NOAELs were not calculated for chromium, silver, and hexachlorobenzene.
- A bird dietary NOAEL was not derived for chlordane.
- A bird egg NOAEL was not derived for DDx.
- Fish dietary LOAELs were not calculated for chromium, lead, and silver.

Unbounded NOAELs are more uncertain than unbounded LOAELs; otherwise, the impact of bounded or unbounded TRVs cannot be determined.

Extrapolation factors were also used to adjust available bird dietary TRVs based on taxonomic differences between the test species and the ecological receptor evaluated. For example, the following are TRVs used in this assessment that were derived in the LPR FFS (USEPA 2014):

- For methylmercury, an interspecies factor of 3 was applied to the toxicity value for mallard ducks, which were assumed to be 3 times less sensitive than the selected avian species evaluated.
- For total LPAH, red-winged blackbirds were assumed to be three times more sensitive than the selected avian species evaluated.
- For total HPAH, pigeons were assumed to be three times less sensitive than selected avian species evaluated.
- For total PCB TEQ, an interspecies extrapolation factor of five was used, because it was assumed that pheasants, the test species, were five times less sensitive than chickens, known to be a highly sensitive species, and the species on which the bird TEFs are based.

The basis for selection of these uncertainty factors and their effect on the risk estimates is described in detail in the LPR FFS (Appendix D, Attachment 6; USEPA 2014). In general, these uncertainty factors are intended to adequately protect virtually all members of the feeding guild represented by the selected receptor species in the conceptual model. The degree to which these TRVs over- or under-estimate risk cannot be quantified.

19.4 Extrapolation of Laboratory-Based TRVs to Wildlife Populations

Laboratory studies are the basis from which TRVs are derived. There are several reasons toxicity tests under laboratory conditions may not represent in-situ toxicity to wildlife populations:

- The adverse effect selected may not occur in all species (i.e., species-specific responses could occur).
- Differences may be present in species sensitivity between test organisms and wildlife.
- Laboratory concentrations and exposure conditions may not be representative of concentrations and conditions to which wildlife in the natural environment are exposed.
    - In laboratory tests, the chemical may be in a more bioavailable form than the form that occurs in the environment.
    - Laboratory tests typically expose the test species to one chemical, while in the natural environment, there is exposure to multiple chemicals at the same time.
    - While lab tests are often short-term exposures, the study design typically employs consistent chemical doses, which may not be representative of wildlife exposures that naturally vary based on foraging behavior and food availability.
- Experimental data are not available for chronic effects on reproduction or growth.
    - Sub-chronic laboratory data often require extrapolation to chronic effect levels using uncertainty factors.
    - Potential population-level effects in the field cannot be inferred from laboratory study effects on individuals other than to presume that the level of protection provided by these TRVs errs on the side of being overly protective.
- Population-level impacts depend on many site-specific factors besides the presence of COPECs (i.e., habitat availability, population age structure, immigration and emigration, reproduction rates, prey availability).

19.5 SSD Tissue TRV Uncertainty

In instances where there were sufficient toxicological data (i.e., five accepted studies or more as determined by the LPRSA BERA), a TRV was developed from an SSD, where the LOAEL TRV was generally selected from the lower tail of the SSD (most often the 5th percentile value). The NOAEL TRV was selected as the highest NOAEL below the LOAEL TRV. This approach is used by USEPA to develop National Ambient Water Quality Criteria and is intended to include the range and distribution of species sensitivities in natural communities, even though these actual sensitivities are unknown and dependent on the communities present. This approach is intended to be less uncertain than TRVs developed from one study by incorporating toxicity data for many species as well as multiple toxicity values for the same species from different studies.

Typically, SSDs are presented as a cumulative distribution function (CDF) of the toxicity of a chemical to a group of laboratory test species. Inherent uncertainties with this approach include: the number of samples and species represented by the SSD and the suitability of the distribution used to fit the SSD (i.e., the best-fit model). The more toxicological data available for the development of the SSD, the more certainty there is in the SSD.

Typically, dose response data are assumed to fit a lognormal distribution, but tools (such as statistical programs that can estimate fit along with a visual examination of the curve and the values at the low end of the distribution) ensure that the most suitable best-fit model available is selected for estimating low-effect thresholds. The use of SSDs as the basis of TRVs was necessarily limited because of the general lack of sufficient toxicological data for most COPECs (e.g., no SSD TRVs could be developed for mammals). The SSD TRVs were obtained from the LPRSA BERA (Windward 2019), which includes further discussion of uncertainties associated with these TRVs; see LPRSA BERA Sections 6.3.3.1 (Methods for Deriving Tissue TRVs), 7.1.3.2 (Selected TRVs for Fish Tissue), 8.1.3.2 (Selected TRVs for Birds), and 8.2.3.2 (Selected TRVs for Bird Eggs).

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